Clinical trial results:
A Phase 3 Randomized, Open Label Study to Evaluate Switching from Regimens Consisting of a Ritonavir-boosted Protease Inhibitor and Two Nucleoside Reverse Transcriptase Inhibitors to Emtricitabine/Rilpivirine/ Tenofovir Disoproxil Fumarate (FTC/RPV/TDF) Fixed-dose Regimen in Virologically Suppressed, HIV-1 Infected Patients

Summary

EudraCT number	2010-023178-37
Trial protocol	GB DE ES BE IT AT
Global end of trial date	28 October 2014

Results information

Result version number	v1 (current)
This version publication date	05 June 2016
First version publication date	05 June 2016

Trial information

Trial identification

Sponsor protocol code	GS-US-264-0106

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01252940
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com
Scientific contact	Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the non-inferiority of emtricitabine 200 mg/rilpivirine 25 mg/tenofovir disoproxil fumarate 300 mg (FTC/RPV/TDF) formulated as a single-tablet regimen (STR) and taken once daily relative to regimens consisting of a ritonavir-boosted protease inhibitor (PI/r) and 2 nucleoside reverse transcriptase inhibitors (NRTIs) in maintaining HIV-1 RNA < 50 copies/mL at Week 24.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 November 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	United Kingdom: 23
Country: Number of subjects enrolled	Austria: 26
Country: Number of subjects enrolled	Belgium: 28
Country: Number of subjects enrolled	France: 43
Country: Number of subjects enrolled	Germany: 43
Country: Number of subjects enrolled	Italy: 26
Country: Number of subjects enrolled	Canada: 25
Country: Number of subjects enrolled	Puerto Rico: 18
Country: Number of subjects enrolled	United States: 230
Worldwide total number of subjects	482
EEA total number of subjects	209

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	477
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 110 sites in the North America and Europe. The first participant was screened on 17 November 2010. The last participant observation was on 28 October 2014.

Pre-assignment

Screening details:

617 participants were screened.

Period 1

Period 1 title	Main Study Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	FTC/RPV/TDF

Arm description:

Participants were randomized to switch from their existing treatment regimen to the emtricitabine (FTC)/rilpivirine (RPV)/tenofovir disoproxil fumarate (TDF) single-tablet regimen (STR) at the beginning of the study.

Arm type	Experimental
Investigational medicinal product name	Emtricitabine/rilpivirine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	Complera®, Eviplera®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Emtricitabine/rilpivirine/tenofovir disoproxil fumarate (FTC/RPV/TDF) 200/25/300 mg single-tablet regimen (STR) administered orally with a meal once daily

Arm title	SBR/Delayed Switch

Arm description:

Participants were randomized to stay on their existing treatment regimen (Stay on Baseline Regimen (SBR)) at the beginning of the study through Week 24, and switch to the FTC/RPV/TDF STR (Delayed Switch) at the Week 24 visit. Their existing treatment regimen consisted of protease inhibitor (PI) + ritonavir (RTV) + 2 two nucleoside reverse transcriptase inhibitors (NRTIs). Protease inhibitors (PIs) may have included amprenavir, atazanavir, darunavir, fosamprenavir, Kaletra (lopinavir/ritonavir, coformulated), ritonavir, and saquinavir. PIs were administered according to prescribing information. Ritonavir (RTV) was administered according to prescribing information. NRTIs may have included abacavir, emtricitabine, Combivir (lamivudine/zidovudine, coformulated), Epzicom (abacavir/lamivudine, coformulated), lamivudine, stavudine, tenofovir DF, Truvada® (emtricitabine/tenofovir DF, coformulated), and zidovudine. NRTIs were administered according to prescribing information.

Arm type	Experimental
Investigational medicinal product name	Emtricitabine/rilpivirine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	Complera®, Eviplera®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

FTC/RPV/TDF 200/25/300 mg STR administered orally with a meal once daily

Number of subjects in period 1[1]	FTC/RPV/TDF	SBR/Delayed Switch
Started	317	159
Completed 24 Weeks (SBR/Delayed Switch)	0 [2]	153
Completed	295	149
Not completed	22	10
Physician decision	1	-
Adverse event, non-fatal	3	1
Subject Non-compliance	1	1
Withdrawal by Subject	6	5
Protocol Violation	4	2
Lost to follow-up	6	1
Lack of efficacy	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 6 participants who were randomized but not treated are not included in the subject disposition table.
NOTE: For the SBR/Delayed Switch group, 152 participants switched regimens at Week 24.
Discontinuations after switch: withdrawal by subject = 2; adverse event = 1; and protocol violation = 1.
[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This milestone only applies to the SBR/Delayed Switch group.

Period 2

Period 2 title	Extension Phase
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	FTC/RPV/TDF

Arm description:

Participants were randomized to switch from their existing treatment regimen to the FTC/RPV/TDF STR at the beginning of the study. Following Week 48, participants may have continued to receive FTC/RPV/TDF STR per protocol before switching to a commercially available source.

Arm type	Experimental
Investigational medicinal product name	Emtricitabine/rilpivirine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	Complera®, Eviplera®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

FTC/RPV/TDF 200/25/300 mg STR administered orally with a meal once daily

Arm title	SBR/Delayed Switch

Arm description:

Participants were randomized to stay on their existing treatment regimen at the beginning of the study through Week 24, and switch to the FTC/RPV/TDF STR (Delayed Switch) at the Week 24 visit. Their existing treatment regimen consisted of PI+RTV+ 2 two NRTIs. PIs may have included amprenavir, atazanavir, darunavir, fosamprenavir, Kaletra (lopinavir/ritonavir, coformulated), ritonavir, and saquinavir. PIs were administered according to prescribing information. RTV was administered according to prescribing information. NRTIs may have included abacavir, emtricitabine, Combivir (lamivudine/zidovudine, coformulated), Epzicom (abacavir/lamivudine, coformulated), lamivudine, stavudine, tenofovir DF, Truvada® (emtricitabine/tenofovir DF, coformulated), and zidovudine. NRTIs were administered according to prescribing information.

Following Week 48, participants may have continued to receive FTC/RPV/TDF STR per protocol before switching to a commercially available source.

Arm type	Experimental
Investigational medicinal product name	Emtricitabine/rilpivirine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	Complera®, Eviplera®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

FTC/RPV/TDF 200/25/300 mg STR administered orally with a meal once daily

Number of subjects in period 2[3]	FTC/RPV/TDF	SBR/Delayed Switch
Started	110	49
Completed	100	46
Not completed	10	3
Physician decision	-	1
Adverse event, non-fatal	2	1
Subject Non-compliance	1	-
Withdrawal by Subject	1	1
Lost to follow-up	5	-
Lack of efficacy	1	-

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: FTC/RPV/TDF group: 110 participants completing the main study continued in extension phase.
SBR/Delayed Switch Group: 49 participants completing the main study continued in extension phase.

Baseline characteristics

Reporting groups	
Reporting group title	FTC/RPV/TDF
Reporting group description:	
Participants were randomized to switch from their existing treatment regimen to the emtricitabine (FTC)/rilpivirine (RPV)/tenofovir disoproxil fumarate (TDF) single-tablet regimen (STR) at the beginning of the study.	
Reporting group title	SBR/Delayed Switch
Reporting group description:	
Participants were randomized to stay on their existing treatment regimen (Stay on Baseline Regimen (SBR)) at the beginning of the study through Week 24, and switch to the FTC/RPV/TDF STR (Delayed Switch) at the Week 24 visit. Their existing treatment regimen consisted of protease inhibitor (PI) + ritonavir (RTV) + 2 two nucleoside reverse transcriptase inhibitors (NRTIs). Protease inhibitors (PIs) may have included amprenavir, atazanavir, darunavir, fosamprenavir, Kaletra (lopinavir/ritonavir, coformulated), ritonavir, and saquinavir. PIs were administered according to prescribing information. Ritonavir (RTV) was administered according to prescribing information. NRTIs may have included abacavir, emtricitabine, Combivir (lamivudine/zidovudine, coformulated), Epzicom (abacavir/lamivudine, coformulated), lamivudine, stavudine, tenofovir DF, Truvada® (emtricitabine/tenofovir DF, coformulated), and zidovudine. NRTIs were administered according to prescribing information.	

Reporting group values	FTC/RPV/TDF	SBR/Delayed Switch	Total
Number of subjects	317	159	476
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	41	43	
standard deviation	± 9.2	± 9.7	-
Gender categorical Units: Subjects			
Female	44	15	59
Male	273	144	417
Ethnicity Units: Subjects			
Hispanic or Latino	51	31	82
Not Hispanic or Latino	264	128	392
Unknown or Not Reported	2	0	2
Race Units: Subjects			
White	241	124	365
Black or African American	61	22	83
American Indian or Alaska Native	3	2	5
Asian	6	2	8
Other	6	9	15
Baseline HIV-1 RNA Category Units: Subjects			
< 50 Copies/mL	299	152	451
50 to < 200 Copies/mL	10	6	16
200 to < 400 Copies/mL	2	0	2
400 to < 1000 Copies/mL	2	0	2

≥ 1000 Copies/mL	4	1	5
Stratification based on antiretroviral (ARV) use Units: Subjects			
TDF or FTC/TDF + lopinavir (LPV) /ritonavir (RTV)	82	49	131
TDF or FTC/TDF + Other PI +RTV	178	81	259
Non-TDF-containing regimen + LPV/RTV	15	9	24
Non-TDF-containing regimen + Other PI+RTV	42	20	62

End points

End points reporting groups

Reporting group title	FTC/RPV/TDF

Reporting group description:

Participants were randomized to switch from their existing treatment regimen to the emtricitabine (FTC)/rilpivirine (RPV)/tenofovir disoproxil fumarate (TDF) single-tablet regimen (STR) at the beginning of the study.

Reporting group title	SBR/Delayed Switch

Reporting group description:

Participants were randomized to stay on their existing treatment regimen (Stay on Baseline Regimen (SBR)) at the beginning of the study through Week 24, and switch to the FTC/RPV/TDF STR (Delayed Switch) at the Week 24 visit. Their existing treatment regimen consisted of protease inhibitor (PI) + ritonavir (RTV) + 2 two nucleoside reverse transcriptase inhibitors (NRTIs). Protease inhibitors (PIs) may have included amprenavir, atazanavir, darunavir, fosamprenavir, Kaletra (lopinavir/ritonavir, coformulated), ritonavir, and saquinavir. PIs were administered according to prescribing information. Ritonavir (RTV) was administered according to prescribing information. NRTIs may have included abacavir, emtricitabine, Combivir (lamivudine/zidovudine, coformulated), Epzicom (abacavir/lamivudine, coformulated), lamivudine, stavudine, tenofovir DF, Truvada® (emtricitabine/tenofovir DF, coformulated), and zidovudine. NRTIs were administered according to prescribing information.

Reporting group title	FTC/RPV/TDF

Reporting group description:

Participants were randomized to switch from their existing treatment regimen to the FTC/RPV/TDF STR at the beginning of the study. Following Week 48, participants may have continued to receive FTC/RPV/TDF STR per protocol before switching to a commercially available source.

Reporting group title	SBR/Delayed Switch

Reporting group description:

Participants were randomized to stay on their existing treatment regimen at the beginning of the study through Week 24, and switch to the FTC/RPV/TDF STR (Delayed Switch) at the Week 24 visit. Their existing treatment regimen consisted of PI+RTV+ 2 two NRTIs. PIs may have included amprenavir, atazanavir, darunavir, fosamprenavir, Kaletra (lopinavir/ritonavir, coformulated), ritonavir, and saquinavir. PIs were administered according to prescribing information. RTV was administered according to prescribing information. NRTIs may have included abacavir, emtricitabine, Combivir (lamivudine/zidovudine, coformulated), Epzicom (abacavir/lamivudine, coformulated), lamivudine, stavudine, tenofovir DF, Truvada® (emtricitabine/tenofovir DF, coformulated), and zidovudine. NRTIs were administered according to prescribing information.

Following Week 48, participants may have continued to receive FTC/RPV/TDF STR per protocol before switching to a commercially available source.

Primary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 (FDA Snapshot Analysis)

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 24 (FDA Snapshot Analysis)

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 24 was analyzed using the FDA snapshot analysis.

Full Analysis Set: participants who were randomized into the study and received at least one dose of study drug.

End point type	Primary

End point timeframe:

Week 24

End point values	FTC/RPV/TDF	SBR/Delayed Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	159		
Units: percentage of participants				
number (not applicable)	93.7	89.9		

Statistical analyses

Statistical analysis title	HIV-1 RNA < 50 Copies/mL at Week 24

Statistical analysis description:

A 95% confidence interval (CI) for the difference between treatment groups in the percentages of virologic success was constructed using normal approximation. Noninferiority was assessed using a conventional 95% CI approach, with a noninferiority margin of 12%. It would be concluded that the FTC/RPV/TDF STR group was not inferior to the SBR group if the lower bound of the 2-sided 95% CI of the difference (FTC/RPV/TDF STR – SBR) in the response rate was greater than -12%.

Comparison groups	FTC/RPV/TDF v SBR/Delayed Switch
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (net)
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	9.1

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 (FDA Snapshot Analysis)

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48 (FDA Snapshot Analysis)

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at Week 48 was analyzed using the FDA snapshot analysis. By Week 48, participants FTC/RPV/TDF had received 48 weeks of treatment with FTC/RPV/TDF, while those in the SBR/Delayed Switch group had received only 24 weeks of treatment with FTC/RPV/TDF.

Participants in the Full Analysis Set in the FTC/RPV/TDF and the Delayed Switch to FTC/RPV/TDF groups were analyzed.

End point type	Secondary

End point timeframe:

Week 48

End point values	FTC/RPV/TDF	SBR/Delayed Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	317	152		
Units: percentage of participants				
number (not applicable)	89.3	92.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Cluster of Differentiation 4 (CD4) Count Through Week 24

End point title	Change From Baseline in Cluster of Differentiation 4 (CD4) Count Through Week 24

End point description:

The mean (SD) change in CD4 count was analyzed from baseline through Week 24.

Participants in the Full Analysis Set who had CD4 measurements at both baseline and Week 24 were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	FTC/RPV/TDF	SBR/Delayed Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	298	148		
Units: cells/mm^3				
arithmetic mean (standard deviation)	20 (± 149.3)	32 (± 158.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4 Count Through Week 48

End point title	Change From Baseline in CD4 Count Through Week 48

End point description:

The mean (SD) change in CD4 count was analyzed from baseline through Week 48. By Week 48, participants FTC/RPV/TDF had received 48 weeks of treatment with FTC/RPV/TDF, while those in the SBR/Delayed Switch group had received only 24 weeks of treatment with FTC/RPV/TDF.

Participants in the Full Analysis Set who had CD4 measurements at both baseline and Week 48 were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	FTC/RPV/TDF	SBR/Delayed Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	143		
Units: cells/mm^3				
arithmetic mean (standard deviation)	10 (± 144.1)	-7 (± 154.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fasting Total Cholesterol Through Week 24

End point title	Change From Baseline in Fasting Total Cholesterol Through Week 24

End point description:

The mean (SD) change from baseline in fasting total cholesterol (mg/dL) through Week 24 was analyzed.

Participants in the Safety Analysis Set who had measurements for total cholesterol at both baseline and Week 24 were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	FTC/RPV/TDF	SBR/Delayed Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	269	134		
Units: mg/dL				
arithmetic mean (standard deviation)	-25 (± 30.2)	-1 (± 25.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fasting Total Cholesterol Through Week 48

End point title	Change From Baseline in Fasting Total Cholesterol Through Week 48

End point description:

The mean (SD) change from baseline in fasting total cholesterol (mg/dL) through Week 48 was analyzed. By Week 48, participants FTC/RPV/TDF had received 48 weeks of treatment with FTC/RPV/TDF, while those in the SBR/Delayed Switch group had received only 24 weeks of treatment with FTC/RPV/TDF.

Participants in the Safety Analysis Set who had measurements for total cholesterol at both baseline and Week 48 were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	FTC/RPV/TDF	SBR/Delayed Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	139		
Units: mg/dL				
arithmetic mean (standard deviation)	-24 (± 32.9)	-24 (± 32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fasting High-density Lipoprotein (HDL) Cholesterol Through Week 24

End point title	Change From Baseline in Fasting High-density Lipoprotein (HDL) Cholesterol Through Week 24

End point description:

The mean (SD) change from baseline in fasting HDL cholesterol (mg/dL) through Week 24 was analyzed.

Participants in the Safety Analysis Set who had measurements for HDL cholesterol at both baseline and Week 24 were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	FTC/RPV/TDF	SBR/Delayed Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	269	134		
Units: mg/dL				
arithmetic mean (standard deviation)	-4 (± 10.3)	-1 (± 8.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fasting HDL Cholesterol Through Week 48

End point title	Change From Baseline in Fasting HDL Cholesterol Through Week 48

End point description:

The mean (SD) change from baseline in fasting HDL cholesterol (mg/dL) through Week 48 was analyzed. By Week 48, participants FTC/RPV/TDF had received 48 weeks of treatment with FTC/RPV/TDF, while those in the SBR/Delayed Switch group had received only 24 weeks of treatment with FTC/RPV/TDF.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	FTC/RPV/TDF	SBR/Delayed Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	139		
Units: mg/dL				
arithmetic mean (standard deviation)	-2 (± 11.6)	-2 (± 8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fasting Direct Low-density Lipoprotein (LDL) Cholesterol Through Week 24

End point title	Change From Baseline in Fasting Direct Low-density Lipoprotein (LDL) Cholesterol Through Week 24

End point description:

The mean (SD) change from baseline in fasting direct LDL cholesterol (mg/dL) through Week 24 was analyzed.

Participants in the Safety Analysis Set who had measurements for direct LDL cholesterol at both baseline and Week 24 were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	FTC/RPV/TDF	SBR/Delayed Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	270	134		
Units: mg/dL				
arithmetic mean (standard deviation)	-16 (± 25.6)	0 (± 23.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fasting Direct LDL Cholesterol Through Week 48

End point title	Change From Baseline in Fasting Direct LDL Cholesterol Through Week 48

End point description:

The mean (SD) change from baseline in fasting direct LDL cholesterol (mg/dL) through Week 48 was analyzed. By Week 48, participants FTC/RPV/TDF had received 48 weeks of treatment with FTC/RPV/TDF, while those in the SBR/Delayed Switch group had received only 24 weeks of treatment with FTC/RPV/TDF.

Participants in the Safety Analysis Set who had measurements for direct LDL cholesterol at both baseline and Week 48 were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	FTC/RPV/TDF	SBR/Delayed Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	139		
Units: mg/dL				
arithmetic mean (standard deviation)	-16 (± 27.1)	-14 (± 26.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fasting Triglycerides Through Week 24

End point title	Change From Baseline in Fasting Triglycerides Through Week 24

End point description:

The mean (SD) change from baseline in fasting triglycerides through Week 24 was analyzed.

Participants in the Safety Analysis Set who had measurements for triglycerides at both baseline and Week 24 were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	FTC/RPV/TDF	SBR/Delayed Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	269	134		
Units: mg/dL				
arithmetic mean (standard deviation)	-53 (± 110)	3 (± 100.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fasting Triglycerides Through Week 48

End point title	Change From Baseline in Fasting Triglycerides Through Week 48

End point description:

The mean (SD) change from baseline in fasting triglycerides through Week 48 was analyzed. By Week 48, participants FTC/RPV/TDF had received 48 weeks of treatment with FTC/RPV/TDF, while those in the SBR/Delayed Switch group had received only 24 weeks of treatment with FTC/RPV/TDF.

Participants in the Safety Analysis Set who had measurements for triglycerides at both baseline and Week 48 were analyzed.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	FTC/RPV/TDF	SBR/Delayed Switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	139		
Units: mg/dL				
arithmetic mean (standard deviation)	-64 (± 126.4)	-80 (± 141.1)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline through end of study (average 54 weeks)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	FTC/RPV/TDF

Reporting group description:

The adverse events reported in this group are those that occurred at any time during the study in participants who were randomized to switch from their existing treatment regimen to the FTC/RPV/TDF STR at the beginning of the study.

Reporting group title	SBR/Delayed Switch (up to Week 24)

Reporting group description:

The adverse events reported in this group are those that occurred in the first 24 weeks of the study in participants who were randomized to stay on their existing treatment regimen (Stay on Baseline Regimen (SBR)) at the beginning of the study and switch to the FTC/RPV/TDF STR (Delayed Switch) at the Week 24 visit.

Reporting group title	SBR/Delayed Switch (After Week 24)

Reporting group description:

The adverse events reported in this group are those that occurred after Week 24 in participants who were randomized to stay on their existing treatment regimen (Stay on Baseline Regimen (SBR)) at the beginning of the study and switch to the FTC/RPV/TDF STR (Delayed Switch) at Week 24 visit.

Serious adverse events	FTC/RPV/TDF	SBR/Delayed Switch (up to Week 24)	SBR/Delayed Switch (After Week 24)
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 317 (6.62%)	8 / 159 (5.03%)	9 / 152 (5.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of thyroid gland			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial occlusive disease			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration			

site conditions			
Chest pain			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 317 (0.32%)	1 / 159 (0.63%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Prostatism			
subjects affected / exposed	0 / 317 (0.00%)	0 / 159 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			

subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bipolar disorder			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Substance-induced mood disorder			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 317 (0.00%)	0 / 159 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	0 / 317 (0.00%)	0 / 159 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stab wound			
subjects affected / exposed	0 / 317 (0.00%)	1 / 159 (0.63%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 317 (0.00%)	0 / 159 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 317 (0.00%)	0 / 159 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sensory loss			
subjects affected / exposed	0 / 317 (0.00%)	0 / 159 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 317 (0.00%)	0 / 159 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Visual acuity reduced			
subjects affected / exposed	0 / 317 (0.00%)	1 / 159 (0.63%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 317 (0.00%)	0 / 159 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephropathy toxic			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis reactive			
subjects affected / exposed	0 / 317 (0.00%)	0 / 159 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Muscular weakness			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyarthritis			
subjects affected / exposed	0 / 317 (0.00%)	1 / 159 (0.63%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 317 (0.95%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute sinusitis			
subjects affected / exposed	0 / 317 (0.00%)	1 / 159 (0.63%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 317 (0.00%)	1 / 159 (0.63%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			

subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shigella infection			
subjects affected / exposed	0 / 317 (0.00%)	1 / 159 (0.63%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 317 (0.00%)	0 / 159 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 317 (0.00%)	1 / 159 (0.63%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 317 (0.32%)	0 / 159 (0.00%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 317 (0.00%)	1 / 159 (0.63%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	FTC/RPV/TDF	SBR/Delayed Switch (up to Week 24)	SBR/Delayed Switch (After Week 24)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	150 / 317 (47.32%)	38 / 159 (23.90%)	59 / 152 (38.82%)
Nervous system disorders			
Headache			
subjects affected / exposed	31 / 317 (9.78%)	6 / 159 (3.77%)	6 / 152 (3.95%)
occurrences (all)	37	6	8
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	22 / 317 (6.94%)	5 / 159 (3.14%)	4 / 152 (2.63%)
occurrences (all)	22	5	4
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	34 / 317 (10.73%)	8 / 159 (5.03%)	6 / 152 (3.95%)
occurrences (all)	37	8	7
Nausea			
subjects affected / exposed	13 / 317 (4.10%)	5 / 159 (3.14%)	10 / 152 (6.58%)
occurrences (all)	13	5	10
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	23 / 317 (7.26%)	1 / 159 (0.63%)	2 / 152 (1.32%)
occurrences (all)	23	1	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	21 / 317 (6.62%)	3 / 159 (1.89%)	9 / 152 (5.92%)
occurrences (all)	21	3	9
Depression			
subjects affected / exposed	18 / 317 (5.68%)	4 / 159 (2.52%)	6 / 152 (3.95%)
occurrences (all)	18	4	6
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	13 / 317 (4.10%)	6 / 159 (3.77%)	8 / 152 (5.26%)
occurrences (all)	16	6	8
Arthralgia			

subjects affected / exposed	18 / 317 (5.68%)	2 / 159 (1.26%)	3 / 152 (1.97%)
occurrences (all)	19	2	3
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	35 / 317 (11.04%)	8 / 159 (5.03%)	12 / 152 (7.89%)
occurrences (all)	44	10	13
Upper respiratory tract infection			
subjects affected / exposed	15 / 317 (4.73%)	5 / 159 (3.14%)	13 / 152 (8.55%)
occurrences (all)	15	5	18

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

There were no limitations affecting the analysis or results.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/2467052