Clinical trial results:
A Phase 3b Randomized, Open Label Study to Evaluate Switching from Regimens Consisting of a Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI) plus Emtricitabine (FTC) and Tenofovir DF (TDF) to the Elvitegravir/Cobicistat/ Emtricitabine/Tenofovir Disoproxil Fumarate Single-Tablet Regimen (EVG/COBI/FTC/TDF) in Virologically Suppressed, HIV 1 Infected Patients

Summary

EudraCT number	2011-004963-56
Trial protocol	GB DE BE AT ES IT
Global end of trial date	01 December 2014

Results information

Result version number	v1 (current)
This version publication date	23 May 2016
First version publication date	23 May 2016

Trial information

Trial identification

Sponsor protocol code	GS-US-236-0121

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01495702
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 Information Desk, Gilead Sciences International Ltd, +44 1223897 496, clinical.trials@gilead.com
Scientific contact	Clinical Trial Information Desk, Gilead Sciences International Ltd, +44 1223897 496, clinical.trials@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	01 December 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the noninferiority of Stribild® (elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate; E/C/F/TDF) single-tablet regimen (STR) relative to regimens consisting of a nonnucleoside reverse transcriptase inhibitor (NNRTI) plus Truvada® (FTC/TDF) in maintaining HIV-1 RNA < 50 copies/mL at Week 48 in virologically suppressed, HIV-1 infected adults.

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	13 December 2011
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	Portugal: 6
Country: Number of subjects enrolled	Spain: 40
Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	Austria: 9
Country: Number of subjects enrolled	Belgium: 21
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 34
Country: Number of subjects enrolled	Italy: 37
Country: Number of subjects enrolled	Canada: 19
Country: Number of subjects enrolled	Australia: 12
Country: Number of subjects enrolled	Puerto Rico: 6
Country: Number of subjects enrolled	United States: 229
Worldwide total number of subjects	439
EEA total number of subjects	173

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)	436
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America, Europe, and Australia. The first participant was screened on 13 December 2011. The last study visit occurred on 01 December 2014.

Pre-assignment

Screening details:

571 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Stribild

Arm description:

Participants switched from their baseline treatment regimen to Stribild STR once daily for up to 96 weeks in the randomized phase, and may have continued to receive Stribild in the extension phase.

Arm type	Experimental
Investigational medicinal product name	Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	Stribild®, EVG/COBI/FTC/TDF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (150/150/200/300 mg) STR once daily

Arm title	NNRTI+FTC/TDF

Arm description:

Participants stayed on their baseline treatment regimen consisting of an nonnucleoside reverse transcriptase inhibitor (NNRTI) (efavirenz (EFV), nevirapine (NVP), or rilpivirine (RPV)) plus emtricitabine (FTC)/TDF (administered according to prescribing information) for up to 96 weeks in the randomized phase, and may have switched to Stribild in the extension phase.

Arm type	Active comparator
Investigational medicinal product name	Emtricitabine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	Truvada®, FTC/TDF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Emtricitabine/tenofovir disoproxil fumarate (200/300 mg) administered according to prescribing information

Number of subjects in period 1[1]	Stribild	NNRTI+FTC/TDF
Started	291	143
Completed	266	119
Not completed	25	24
Withdrew Consent	10	18
Adverse event, non-fatal	2	2
Participant Noncompliance	1	-
Death	1	-
Lost to Follow-up	4	3
Investigators Discretion	2	-
Protocol Violation	3	1
Lack of efficacy	2	-

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: 5 participants who were enrolled but not treated are not included in the subject disposition table.

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Stribild

Arm description:

Participants switched from their baseline treatment regimen to Stribild® (elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate; E/C/F/TDF) (150/150/200/300 mg) single-tablet regimen (STR) once daily for up to 96 weeks in the randomized phase, and may have continued to receive Stribild in the extension phase.

Arm type	Experimental
Investigational medicinal product name	Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	Stribild®, EVG/COBI/FTC/TDF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (150/150/200/300 mg) STR once daily

Arm title	NNRTI+FTC/TDF

Arm description:

Participants stayed on their baseline treatment regimen consisting of an nonnucleoside reverse transcriptase inhibitor (NNRTI) (efavirenz (EFV), nevirapine (NVP), or rilpivirine (RPV)) plus emtricitabine (FTC)/TDF (administered according to prescribing information) for up to 96 weeks in the randomized phase, and may have switched to Stribild in the extension phase.

Arm type	Active comparator

Investigational medicinal product name	Emtricitabine/tenofovir disoproxil fumarate
Investigational medicinal product code	
Other name	Truvada®, FTC/TDF
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Emtricitabine/tenofovir disoproxil fumarate (200/300 mg) administered according to prescribing information

Number of subjects in period 2[2]	Stribild	NNRTI+FTC/TDF
Started	26	2
Completed	26	2

Notes:

[2] - 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: Of those who completed the Randomized Phase (Stribild: n = 291; NNRTI+FTC/TDF: n = 143), 26 participants randomized to Stribild and 2 participants randomized to NNRTI+FTC/TDF entered the Extension Phase.

Baseline characteristics

Reporting groups	
Reporting group title	Stribild
Reporting group description:	
Participants switched from their baseline treatment regimen to Stribild STR once daily for up to 96 weeks in the randomized phase, and may have continued to receive Stribild in the extension phase.	
Reporting group title	NNRTI+FTC/TDF
Reporting group description:	
Participants stayed on their baseline treatment regimen consisting of an nonnucleoside reverse transcriptase inhibitor (NNRTI) (efavirenz (EFV), nevirapine (NVP), or rilpivirine (RPV)) plus emtricitabine (FTC)/TDF (administered according to prescribing information) for up to 96 weeks in the randomized phase, and may have switched to Stribild in the extension phase.	

Reporting group values	Stribild	NNRTI+FTC/TDF	Total
Number of subjects	291	143	434
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	42	40	
standard deviation	± 9.6	± 9.7	-
Gender categorical Units: Subjects			
Female	23	9	32
Male	268	134	402
Race Units: Subjects			
American Indian or Alaska Native	2	0	2
Asian	4	9	13
Black or African Heritage	49	23	72
Native Hawaiian or Pacific Islander	1	0	1
White	231	109	340
Other	4	2	6
Ethnicity Units: Subjects			
Hispanic/Latino	30	16	46
Non-Hispanic/Latino	261	127	388
HIV-1 RNA Category Units: Subjects			
< 50 copies/mL	285	141	426
50 to < 200 copies/mL	4	2	6
200 to < 400 copies/mL	0	0	0
≥ 400 copies/mL	2	0	2
CD4+ Cell Count Category Units: Subjects			
≤ 50 cells/µL	0	0	0
51 to ≤ 200 cells/µL	4	1	5
201 to ≤ 350 cells/µL	26	20	46

351 to ≤ 500 cells/µL	75	33	108
> 500 cells/µL	186	89	275
HIV Disease Status Units: Subjects			
Asymptomatic	225	115	340
Symptomatic HIV Infections	36	14	50
AIDS	30	14	44
CD4+ Cell Count Units: cells/µL			
arithmetic mean	586	593	
standard deviation	± 210.3	± 224.6	-

End points

End points reporting groups

Reporting group title	Stribild
Reporting group description:	
Participants switched from their baseline treatment regimen to Stribild STR once daily for up to 96 weeks in the randomized phase, and may have continued to receive Stribild in the extension phase.	
Reporting group title	NNRTI+FTC/TDF
Reporting group description:	
Participants stayed on their baseline treatment regimen consisting of an nonnucleoside reverse transcriptase inhibitor (NNRTI) (efavirenz (EFV), nevirapine (NVP), or rilpivirine (RPV)) plus emtricitabine (FTC)/TDF (administered according to prescribing information) for up to 96 weeks in the randomized phase, and may have switched to Stribild in the extension phase.	
Reporting group title	Stribild
Reporting group description:	
Participants switched from their baseline treatment regimen to Stribild® (elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate; E/C/F/TDF) (150/150/200/300 mg) single-tablet regimen (STR) once daily for up to 96 weeks in the randomized phase, and may have continued to receive Stribild in the extension phase.	
Reporting group title	NNRTI+FTC/TDF
Reporting group description:	
Participants stayed on their baseline treatment regimen consisting of an nonnucleoside reverse transcriptase inhibitor (NNRTI) (efavirenz (EFV), nevirapine (NVP), or rilpivirine (RPV)) plus emtricitabine (FTC)/TDF (administered according to prescribing information) for up to 96 weeks in the randomized phase, and may have switched to Stribild in the extension phase.	

Primary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 48
End point description:	
• The FDA-defined Snapshot algorithm was used, which defines a patient's virologic response status using only the viral load at the predefined time point within an allowed window of time. • Analysis Population Description: Full analysis set includes randomized subjects who took at least one dose of study drug, had no documented resistance and were on NNRTI at screening.	
End point type	Primary
End point timeframe:	
Week 48	

End point values	Stribild	NNRTI+FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	143		
Units: percentage of participants				
number (not applicable)	93.4	88.1		

Statistical analyses

Statistical analysis title	Difference in proportions

Statistical analysis description:

The null hypothesis was that the Stribild group was at least 12% worse than the NNRTI+FTC/TDF group with respect to the percentage of participants maintaining HIV-1 RNA < 50 copies/mL at Week 48. The alternative hypothesis was that the Stribild group was less than 12% worse than the NNRTI+FTC/TDF group.

Comparison groups	Stribild v NNRTI+FTC/TDF
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.066
Method	Fisher exact
Parameter estimate	Difference in proportions
Point estimate	5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	12

Notes:

[1] - The 95% confidence interval (CI) for the difference was from unconditional exact method using 2 inverted 1-sided tests with the standardized statistic using StatXact.

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Week 96
End point description:	
Full Analysis Set	
End point type	Secondary
End point timeframe:	
Week 96	

End point values	Stribild	NNRTI+FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290	143		
Units: percentage of participants				
number (not applicable)	86.6	80.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4+ Cell Count at Week 48

End point title	Change From Baseline in CD4+ Cell Count at Week 48
End point description:	
Full Analysis Set	
End point type	Secondary

End point timeframe:
Baseline; Week 48

End point values	Stribild	NNRTI+FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	270	126		
Units: cells/µL				
arithmetic mean (standard deviation)	56 (± 147.3)	58 (± 179.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4+ Cell Count at Week 96

End point title	Change From Baseline in CD4+ Cell Count at Week 96
End point description: Full Analysis Set	
End point type	Secondary
End point timeframe: Baseline; Week 96	

End point values	Stribild	NNRTI+FTC/TDF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	116		
Units: cells/µL				
arithmetic mean (standard deviation)	83 (± 166.7)	101 (± 156.5)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline through end of study drug treatment (average exposure = 90 weeks) plus 30 days

Adverse event reporting additional description:

Safety Analysis Set participants were randomized and received at least 1 dose of study drug

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Stribild

Reporting group description:

Adverse events for this reporting group include those occurring in participants receiving Stribild in the randomized phase.
Participants switched from their baseline treatment regimen to Stribild (E/C/F/TDF) (150/150/200/300 mg) STR once daily for up to 96 weeks in the randomized phase, and may have continued to receive Stribild in the extension phase.

Reporting group title	NNRTI+FTC/TDF

Reporting group description:

Adverse events for this reporting group include those occurring in participants receiving NNRTI+FTC/TDF in the randomized phase.
Participants stayed on their baseline treatment regimen consisting of an NNRTI (EFV, NVP, or RPV) plus FTC/ TDF (200/300 mg) (administered according to prescribing information) for up to 96 weeks in the randomized phase, and may have switched to Stribild in the extension phase.

Reporting group title	All Stribild

Reporting group description:

Adverse events for this reporting group include those occurring in all participants while receiving Stribild in the randomized and extension phases.

Serious adverse events	Stribild	NNRTI+FTC/TDF	All Stribild
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 291 (8.25%)	7 / 143 (4.90%)	26 / 293 (8.87%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			

subjects affected / exposed	0 / 291 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to liver			
subjects affected / exposed	0 / 291 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 291 (0.00%)	1 / 143 (0.70%)	0 / 293 (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
Hypertensive crisis			
subjects affected / exposed	0 / 291 (0.00%)	1 / 143 (0.70%)	0 / 293 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
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	0 / 291 (0.00%)	1 / 143 (0.70%)	0 / 293 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hypersensitivity			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 291 (0.00%)	1 / 143 (0.70%)	0 / 293 (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
Pulmonary embolism			
subjects affected / exposed	0 / 291 (0.00%)	1 / 143 (0.70%)	0 / 293 (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
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Delusion			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Drug abuse			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Substance-induced psychotic disorder			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rib fracture			
subjects affected / exposed	0 / 291 (0.00%)	1 / 143 (0.70%)	0 / 293 (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			
Myocardial infarction			
subjects affected / exposed	1 / 291 (0.34%)	2 / 143 (1.40%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Psychomotor hyperactivity			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 291 (0.00%)	1 / 143 (0.70%)	0 / 293 (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
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 291 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 291 (0.00%)	1 / 143 (0.70%)	0 / 293 (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
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Renal failure acute			
subjects affected / exposed	1 / 291 (0.34%)	1 / 143 (0.70%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Septic shock			
subjects affected / exposed	1 / 291 (0.34%)	1 / 143 (0.70%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 291 (0.00%)	2 / 143 (1.40%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shigella infection			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Urosepsis			
subjects affected / exposed	1 / 291 (0.34%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 291 (0.00%)	1 / 143 (0.70%)	0 / 293 (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	Stribild	NNRTI+FTC/TDF	All Stribild
Total subjects affected by non-serious adverse events			
subjects affected / exposed	154 / 291 (52.92%)	66 / 143 (46.15%)	154 / 293 (52.56%)
Nervous system disorders			
Headache			
subjects affected / exposed	29 / 291 (9.97%)	8 / 143 (5.59%)	29 / 293 (9.90%)
occurrences (all)	29	8	29
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	19 / 291 (6.53%)	2 / 143 (1.40%)	19 / 293 (6.48%)
occurrences (all)	23	2	23
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	30 / 291 (10.31%)	11 / 143 (7.69%)	30 / 293 (10.24%)
occurrences (all)	33	12	33
Nausea			
subjects affected / exposed	24 / 291 (8.25%)	4 / 143 (2.80%)	24 / 293 (8.19%)
occurrences (all)	25	4	25
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	24 / 291 (8.25%)	5 / 143 (3.50%)	24 / 293 (8.19%)
occurrences (all)	32	6	32
Psychiatric disorders			

Insomnia			
subjects affected / exposed	22 / 291 (7.56%)	11 / 143 (7.69%)	22 / 293 (7.51%)
occurrences (all)	22	11	22
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	23 / 291 (7.90%)	8 / 143 (5.59%)	23 / 293 (7.85%)
occurrences (all)	23	8	23
Arthralgia			
subjects affected / exposed	19 / 291 (6.53%)	5 / 143 (3.50%)	19 / 293 (6.48%)
occurrences (all)	19	6	19
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	33 / 291 (11.34%)	15 / 143 (10.49%)	33 / 293 (11.26%)
occurrences (all)	41	19	41
Sinusitis			
subjects affected / exposed	21 / 291 (7.22%)	5 / 143 (3.50%)	21 / 293 (7.17%)
occurrences (all)	23	5	23
Syphilis			
subjects affected / exposed	17 / 291 (5.84%)	10 / 143 (6.99%)	17 / 293 (5.80%)
occurrences (all)	19	10	19
Nasopharyngitis			
subjects affected / exposed	30 / 291 (10.31%)	17 / 143 (11.89%)	30 / 293 (10.24%)
occurrences (all)	41	24	41

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 December 2011	• Extended the study from 48 to 96 weeks and removed the switch to STB at Week 48 for subjects in Treatment Group 2 based on feedback from the US Food and Drug Administration (FDA); updated Study Schema • Updated secondary study objectives based on feedback from the US FDA • Clarified and updated the inclusion and exclusion criteria • Updated the Table of Disallowed and Discouraged Medications to reflect draft STB label
27 June 2012	• Updated inclusion criteria to allow subjects to be on their first or second ARV drug regimen (to be more reflective of the target patient population), to change estimated glomerular filtration rate (eGFR) entry criteria from ≥ 90 mL/min to ≥ 70 mL/min, and to clarify that subjects could be rescreened with approval from the medical monitor • Clarified the duration of the study throughout the protocol • Clarified the thymidine analog-associated mutations • Updated the screening visit procedures to align with the directive of DSPH group • Updated the CT3 guidance in Section 7.4 (as outlined in Administrative Letter 2) • Updated the new contact information for DSPH and remove requirement to email safety event reports due to restrictive data privacy laws in some countries • Changed the after study reporting requirements • Updated the definitions of childbearing potential, postmenopausal, and contraception requirements • Updated Study Procedures Table footnotes

Notes:

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: