Clinical trial results:
A Multicenter, Randomized, Blinded, Placebo-Controlled Study to Evaluate the Safety of Maraviroc in Combination With Other Antiretroviral Agents in HIV-1-Infected Subjects Co-Infected with Hepatitis C and/or Hepatitis B Virus.

Summary

EudraCT number	2010-021994-35
Trial protocol	HU CZ DE GB ES
Global end of trial date	24 March 2015

Results information

Result version number	v1 (current)
This version publication date	02 April 2016
First version publication date	02 April 2016

Trial information

Trial identification

Sponsor protocol code	A4001098

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01327547
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ViiV Healthcare UK Limited
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom, TW8 9GS
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 800 718 1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 800 718 1021, ClinicalTrials.gov_Inquiries@pfizer.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	09 October 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the incidence of Grade 3 and Grade 4 ALT abnormalities defined as >5x ULN for subjects whose baseline ALT ≤ULN, or >3.5x baseline for subjects whose baseline ALT >ULN, at Week 48 in the Maraviroc (MVC) versus the Placebo (PBO) arm.

Protection of trial subjects:

All parties will ensure protection of subject personal data and will not include subject names on any sponsor forms, reports, publications, or in any other disclosures, except where required by laws. Subject names, address, birth date and other identifiable data will be replaced by an alpha-numerical code consisting of a numbering system provided by Pfizer and year of birth. In case of data transfer, ViiV Healthcare or its designated representative will maintain high standards of confidentiality and protection of subject personal data.

The informed consent form must be in compliance with ICH GCP, local regulatory requirements, and legal requirements.

The informed consent form used in this study, and any changes made during the course of the study, must be prospectively approved by both the IRB/IEC and Pfizer before use.

Background therapy: -

Evidence for comparator:

None

Actual start date of recruitment	18 May 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 5
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	Puerto Rico: 4
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	United States: 57
Country: Number of subjects enrolled	United Kingdom: 4
Worldwide total number of subjects	137
EEA total number of subjects	76

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)	135
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In this study, 138 participants were randomized, of which 137 participants received the study drug. Participants were randomized at 37 sites in 9 countries. Five sites received drug and screened participants but did not randomize any participants; 2 sites received drug but did not screen any subjects.

Pre-assignment

Screening details:

One participant who was randomized into the study was withdrawn prior to receiving treatment due to poor venous access.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Maraviroc

Arm description:

Participants who received maraviroc in combination with Highly active antiretroviral therapy (HAART)

Arm type	Experimental
Investigational medicinal product name	Maraviroc
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Maraviroc tablets were supplied as 150 mg or 300 mg dosage units. Drug supplies were provided to the investigator sites as pre packaged bottles containing 70 tablets per bottle.

Arm title	Placebo

Arm description:

Participants who received placebo in combination with HAART

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets were supplied as 150 mg or 300 mg dosage units. Drug supplies were provided to the investigator sites as pre packaged bottles containing 70 tablets per bottle.

Number of subjects in period 1	Maraviroc	Placebo
Started	70	67
Completed	50	45
Not completed	20	22
Adverse event, serious fatal	1	2
Required prohibited medication	2	-
Non-compliance due to alcohol intake	-	1
Consent withdrawn by subject	3	7
Does Not Meet Entrance Criteria	2	2
Adverse event, non-fatal	4	1
Non-Compliance With Study Treatment	-	2
By investigator in subject's interest	-	1
Lost to follow-up	6	6
Protocol deviation	1	-
Non-compliance with study procedures	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Maraviroc
Reporting group description:	
Participants who received maraviroc in combination with Highly active antiretroviral therapy (HAART)	
Reporting group title	Placebo
Reporting group description:	
Participants who received placebo in combination with HAART	

Reporting group values	Maraviroc	Placebo	Total
Number of subjects	70	67	137
Age categorical Units: Subjects			
<18 years	0	0	0
18-44 years	26	20	46
45-64 years	42	47	89
>=65 years	2	0	2
Age continuous Units: years			
arithmetic mean	47.9	48.7	
standard deviation	± 9	± 7.2	-
Gender, Male/Female Units: Participants			
Female	10	10	20
Male	60	57	117

End points

End points reporting groups

Reporting group title	Maraviroc
Reporting group description:	
Participants who received maraviroc in combination with Highly active antiretroviral therapy (HAART)	
Reporting group title	Placebo
Reporting group description:	
Participants who received placebo in combination with HAART	
Subject analysis set title	Maraviroc 150 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received Maraviroc 150 mg twice a day (BID) in combination with a potent CYP3A4 inhibitor. Participants included in the statistical analysis of pharmacokinetic (PK) parameters were those with the PK parameter of interest. Analysis sets could contain different numbers of participants for different PK parameters based on availability of the data. Data from studies A4001098 have been pooled for this analysis.Note: subject analysis set only applies to PK related result report	
Subject analysis set title	Maraviroc 300 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received Maraviroc 300 mg BID in the absence of a potent CYP3A4 inhibitor and inducer.Participants included in the statistical analysis of PK parameters were those with the PK parameter of interest. Analysis sets could contain different numbers of participants for different PK parameters based on availability of the data. Data from studies A4001098 have been pooled for this analysis. Note: subject analysis set only applies to PK related result report.	
Subject analysis set title	Maraviroc 600 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received Maraviroc 600 mg BID in the absence of a potent CYP3A4 inhibitor and inducer.Participants included in the statistical analysis of PK parameters were those with the PK parameter of interest. Analysis sets could contain different numbers of participants for different PK parameters based on availability of the data. Data from studies A4001098 have been pooled for this analysis. Note: subject analysis set only applies to PK related result report.	
Subject analysis set title	Aspartate transaminase (AST)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who received maraviroc 150 mg, or maraviroc 300 mg, or maraviroc 600 mg and had Cavg data and laboratory results available at week 48. Last observation carried forward (LOCF) was utilized if the Week 48 time point was missing for any pharmacodynamic (PD) assessment. Note: subject analysis set only applies to PK related result report.	
Subject analysis set title	Alanine transaminase (ALT)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who received maraviroc 150 mg, or maraviroc 300 mg, or maraviroc 600 mg and had Cavg data and laboratory results available at week 48. LOCF was utilized if the Week 48 time point was missing for any PD assessment. Note: subject analysis set only applies to PK related result report.	
Subject analysis set title	Bilirubin (BIL)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who received maraviroc 150 mg, or maraviroc 300 mg, or maraviroc 600 mg and had Cavg data and laboratory results available at week 48. LOCF was utilized if the Week 48 time point was missing for any PD assessment. Note: subject analysis set only applies to PK related result report.	
Subject analysis set title	Enhanced Liver Fibrosis (ELF)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who received maraviroc 150 mg, or maraviroc 300 mg, or maraviroc 600 mg and had Cavg	

data and laboratory results available at week 48. LOCF was utilized if the Week 48 time point was missing for any PD assessment. Note: subject analysis set only applies to PK related result report.

Subject analysis set title	Fibroscan (FSCN)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received maraviroc 150 mg, or maraviroc 300 mg, or maraviroc 600 mg and had Cavg data and elastography results available at week 48. LOCF was utilized if the Week 48 time point was missing for any PD assessment. Hepatic elastography was only done at sites that had Fibroscan® equipment. Note: subject analysis set only applies to PK related result report.

Subject analysis set title	Alkaline phosphatase (ALK)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received maraviroc 150 mg, or maraviroc 300 mg, or maraviroc 600 mg and had Cavg data and laboratory results available at week 48. LOCF was utilized if the Week 48 time point was missing for any PD assessment. Note: subject analysis set only applies to PK related result report.

Primary: Percentage of participants with Grade 3 and Grade 4 alanine aminotransferase (ALT) abnormalities at Week 48

End point title	Percentage of participants with Grade 3 and Grade 4 alanine aminotransferase (ALT) abnormalities at Week 48

End point description:

Percentage of participants with Grade 3 or Grade 4 ALT abnormalities defined as >5x upper limit of normal (ULN) for participants whose baseline ALT ≤ULN, or >3.5x baseline for participants whose baseline ALT >ULN, up to and including Week 48 in the maraviroc arm versus the placebo arm. The baseline was defined as the last measurement prior to Day 1 dosing.

End point type	Primary

End point timeframe:

48 weeks

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: Percentage of participants				
number (not applicable)	1.4	1.5		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 48

Statistical analysis description:

A stratified analysis was conducted by summarizing the difference in proportions adjusted for the randomization strata formed by crossing levels of stratification variables. 2 of the 3 protocol-defined randomization strata, HBV status and PI-based regimen were used in analyses of primary and secondary endpoints as appropriate. The third randomization stratum, participation in the liver biopsy sub-study, was not used as a covariate. The Cochran-Mantel-Haenszel (CMH) approach was used.

Comparison groups	Maraviroc v Placebo

Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.4598
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-0.002
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0417
upper limit	0.0376

Secondary: Percentage of participants with Grade 3 and Grade 4 ALT abnormalities through Week 144

End point title	Percentage of participants with Grade 3 and Grade 4 ALT abnormalities through Week 144

End point description:

Percentage of participants with Grade 3 or Grade 4 ALT abnormalities defined as >5x upper limit of normal (ULN) for participants whose baseline ALT ≤ULN, or >3.5x baseline for participants whose baseline ALT >ULN, up to and including Week 96 and Week 144 in the maraviroc arm versus the placebo arm. The baseline was defined as the last measurement prior to Day 1 dosing.

End point type	Secondary

End point timeframe:

Week 96 and Week 144

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: Percentage of participants				
number (not applicable)				
at Week 96	1.4	3		
at Week 144	2.9	4.5		

Statistical analyses

Statistical analysis title	Statitical analysis at Week 96
Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	-0.0167

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0653
upper limit	0.0319

Statistical analysis title	Statistical analysis at Week 144
Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.0177
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0805
upper limit	0.0452

Secondary: Time to development of Grade 3 and Grade 4 ALT abnormalities

End point title	Time to development of Grade 3 and Grade 4 ALT abnormalities

End point description:

Time taken in days to development of Grade 3 and Grade 4 ALT abnormalities defined as >5x ULN for participants whose baseline ALT ≤ULN, or >3.5x baseline for participants whose baseline ALT >ULN, at Week 144.

End point type	Secondary

End point timeframe:

144 weeks

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: Days				
median (confidence interval)	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Grade 3 and Grade 4 ALT abnormalities associated with a change from baseline ALT >100 IU/L

End point title	Percentage of participants with Grade 3 and Grade 4 ALT abnormalities associated with a change from baseline ALT >100 IU/L

End point description:

Percentage of participants who had Grade 3 and Grade 4 ALT abnormalities associated with a change from baseline ALT >100 IU/L during the 144-week period. Baseline will be defined as the last measurement prior to Day 1 dosing.

End point type	Secondary

End point timeframe:

144 weeks

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: Percentage of participants				
number (not applicable)				
Grade 3	2.8	4.4		
Grade 4	1.4	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to development of Grade 3 and Grade 4 ALT abnormalities at Week 144 associated with a change from baseline ALT >100 IU/L

End point title	Time to development of Grade 3 and Grade 4 ALT abnormalities at Week 144 associated with a change from baseline ALT >100 IU/L

End point description:

Time to development of Grade 3 and Grade 4 ALT abnormalities associated with a change from baseline ALT >100 IU/L during the 144-week period. Baseline will be defined as the last measurement prior to Day 1 dosing.

End point type	Secondary

End point timeframe:

144 weeks

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: Days				
median (confidence interval 95%)	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Hy's law abnormalities through Week 144

End point title	Number of participants with Hy's law abnormalities through Week 144

End point description:

Hy’s law was defined as a total bilirubin >2x ULN with a simultaneous ALT or aspartate transaminase (AST)>3x ULN, excluding participants with an alkaline phosphatase>3x ULN

End point type	Secondary

End point timeframe:

144 weeks

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with plasma human immunodeficiency virus (HIV)-1 ribonucleic acid (RNA) concentration <40 copies/mL at Week 48, 96 and 144

End point title	Percentage of participants with plasma human immunodeficiency virus (HIV)-1 ribonucleic acid (RNA) concentration <40 copies/mL at Week 48, 96 and 144

End point description:

The Food and Drug Administration (FDA) snapshot algorithm was used to derive the efficacy endpoint of the proportion of participants with HIV-1 RNA <40 copies/mL at Week 48, 96 and 144 . This algorithm included the missing data imputation method and used the plasma HIV-1 RNA concentration in the visit window only, followed the “virology-first principle” and considered a participant who had a missing plasma HIV-1 RNA concentration, or switched to a prohibited background anti-retroviral regimen or discontinues from the study or study drug as a failure (MSDF).

End point type	Secondary

End point timeframe:

Week 48, 96 and 144

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: Percentage of participants				
number (not applicable)				
Week 48	77.1	79.1		

Week 96	67.1	70.1		
Week 144	58.6	67.2		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 48

Statistical analysis description:

A stratified analysis was conducted by summarizing the difference in proportions adjusted for the randomization strata formed by crossing levels of stratification variables. The CMH approach was used. No formal hypothesis test was performed. Week 48 data presented here.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in proportion
Point estimate	-0.015
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1484
upper limit	0.1185

Statistical analysis title	Statistical analysis at Week 96

Statistical analysis description:

A stratified analysis was conducted by summarizing the difference in proportions adjusted for the randomization strata formed by crossing levels of stratification variables. The CMH approach was used. No formal hypothesis test was performed. Week 96 data presented here.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.0255
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1784
upper limit	0.1274

Statistical analysis title	Statistical analysis at Week 144

Statistical analysis description:

A stratified analysis was conducted by summarizing the difference in proportions adjusted for the randomization strata formed by crossing levels of stratification variables. The CMH approach was used. No formal hypothesis test was performed. Week 144 data presented here.

Comparison groups	Maraviroc v Placebo

Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.083
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2421
upper limit	0.0761

Secondary: Mean change from baseline in CD4+ and CD8+ cell counts at Week 48, 96 and 144

End point title	Mean change from baseline in CD4+ and CD8+ cell counts at Week 48, 96 and 144

End point description:

Immunologic response (magnitude of change in CD4+ and CD8+ cell counts from baseline) was measured. Baseline value for CD4 and CD8 is defined as the pre-dose measurement taken at Day 1 visit.

End point type	Secondary

End point timeframe:

Week 48, 96 and 144

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	67		
Units: Cells/µL				
arithmetic mean (standard deviation)				
CD4+ (week 48, n=69, 67)	3.1 (± 142.58)	42 (± 166.35)		
CD8+ (week 48, n=69, 67)	7.8 (± 229.53)	28.9 (± 293.18)		
CD4+ (week 96, n=69, 67)	5.1 (± 146.64)	49.7 (± 177.18)		
CD8+ (week 96, n=69, 67)	-2.7 (± 228.92)	62.6 (± 376.67)		
CD4+ (week 144, n=69, 67)	17.2 (± 184.86)	41.7 (± 200)		
CD8+ (week 144, n=69, 67)	12.6 (± 293.82)	44.1 (± 387.61)		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 48

Statistical analysis description:

The above analysis is for CD4+ cells at week 48. Results are from an analysis of covariance (ANCOVA) model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, hepatitis B virus status

(HBV), Protease inhibitor (PI)-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1174 [1]
Method	ANCOVA
Parameter estimate	Difference in Least Square (LS) Mean
Point estimate	-41.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-92.72
upper limit	10.49

Notes:

[1] - Not specified.

Statistical analysis title	Statistical analysis at Week 48

Statistical analysis description:

The above analysis is for CD8+ cells at Week 48. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, hepatitis B virus status (HBV), Protease inhibitor (PI)-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.593 [2]
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-21.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-103.05
upper limit	59.12

Notes:

[2] - Not specified.

Statistical analysis title	Statistical analysis at Week 96

Statistical analysis description:

The above analysis is for CD4+ cells at Week 96. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, hepatitis B virus status (HBV), Protease inhibitor (PI)-based regimen.

Comparison groups	Maraviroc v Placebo

Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0669
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-48.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99.93
upper limit	3.41

Statistical analysis title	Statistical analysis at Week 144

Statistical analysis description:

The above analysis is for CD4+ cells at Week 144. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, hepatitis B virus status (HBV), Protease inhibitor (PI)-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3859
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-27.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-90.71
upper limit	35.29

Statistical analysis title	Statistical analysis at Week 96

Statistical analysis description:

The above analysis is for CD8+ cells at Week 96. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, hepatitis B virus status (HBV), Protease inhibitor (PI)-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1799
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-65.28

Confidence interval	
level	95 %
sides	2-sided
lower limit	-161.07
upper limit	30.5

Statistical analysis title	Statistical analysis at Week 144

Statistical analysis description:

The above analysis is for CD8+ cells at Week 144. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, hepatitis B virus status (HBV), Protease inhibitor (PI)-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5571
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-31.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-138.93
upper limit	75.21

Secondary: Mean change from baseline in CD38 expression on CD4 and CD8 cells at Weeks 48, 96 and 144

End point title	Mean change from baseline in CD38 expression on CD4 and CD8 cells at Weeks 48, 96 and 144

End point description:

Plasma samples were used to determine markers of immune activation namely CD38 expression on CD4 and CD8 cells.

End point type	Secondary

End point timeframe:

48, 96 and 144 weeks

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	67		
Units: cell/mm³				
arithmetic mean (standard deviation)				
Week 48 (n=69, 67)	-12.2 (± 129.82)	43 (± 135.71)		

Week 96 (n=69, 67)	5.4 (± 134.64)	47.4 (± 186.74)		
Week 144(n=69, 67)	23.4 (± 169.5)	50.7 (± 219.95)		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 48

Statistical analysis description:

The above analysis is for CD38 expression on CD4 and CD8 cells at Week 48. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0153 [3]
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-56.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-101.2
upper limit	-10.92

Notes:

[3] - Not specified.

Statistical analysis title	Statistical analysis at Week 96

Statistical analysis description:

The above analysis is for CD38 expression on CD4 and CD8 cells for Week 96. Results were from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0947
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-44.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-97.72
upper limit	7.87

Statistical analysis title	Statistical analysis at Week 144

Statistical analysis description:

The above analysis is for CD38 expression on CD4 and CD8 cells for Week 144. Results were from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3595
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-29.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-93.74
upper limit	34.24

Secondary: Mean change from baseline in markers of immune activation: C-reactive protein (CRP) - Week 48, 96 and 144.

End point title	Mean change from baseline in markers of immune activation: C-reactive protein (CRP) - Week 48, 96 and 144.

End point description:

Plasma samples were used to determine markers of immune activation namely CRP.

End point type	Secondary

End point timeframe:

48, 96 and 144 weeks

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 48 (n=70, 67)	0.4 (± 8.18)	3.1 (± 26.66)		
Week 96 (n=70, 67)	0 (± 5.16)	-0.7 (± 3.32)		
Week 144 (n=70, 67)	0.6 (± 7.99)	-0.3 (± 5.28)		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 48

Statistical analysis description:

The above analysis is for C-reactive protein cells at Week 48. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment

(Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4476 [4]
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-2.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.11
upper limit	4.05

Notes:

[4] - Not specified.

Statistical analysis title	Statistical analysis at Week 96

Statistical analysis description:

The above analysis is for C-reactive protein cells at Week 96. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3012
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	1.96

Statistical analysis title	Statistical analysis at Week 144

Statistical analysis description:

The above analysis is for C-reactive protein cells at Week 144. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4196
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	0.92

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.33
upper limit	3.17

Secondary: Mean change from baseline in markers of immune activation: D dimer - Week 48, 96 and 144

End point title	Mean change from baseline in markers of immune activation: D dimer - Week 48, 96 and 144

End point description:

Plasma samples were used to determine markers of immune activation namely D-Dimer.

End point type	Secondary

End point timeframe:

48, 96 and 144 weeks

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: ng/dL				
arithmetic mean (standard deviation)				
Week 48 (n= 68, 65)	-101.1 (± 753.24)	-20.4 (± 215.62)		
Week 96 (n= 68, 65)	-88.1 (± 740.14)	-23.1 (± 201.55)		
Week 144 (n= 68, 65)	-97.4 (± 768.98)	9.8 (± 358.07)		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 48

Statistical analysis description:

The above analysis is for D-Dimer cells at Week 48. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9904
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-48.66
upper limit	49.26

Statistical analysis title	Statistical analysis at Week 96

Statistical analysis description:

The above analysis is for D-Dimer cells at Week 96. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7697
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	10.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.44
upper limit	84.18

Statistical analysis title	Statistical analysis at Week 144

Statistical analysis description:

The above analysis is for D-Dimer cells at Week 144. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5816
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-24.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-112.21
upper limit	63.23

Secondary: Mean change from baseline in markers of immune activation:

Transforming growth factor-beta (TGF beta) - Week 48, 96 and 144	
End point title	Mean change from baseline in markers of immune activation: Transforming growth factor-beta (TGF beta) - Week 48, 96 and 144

End point description:

Plasma samples were used to determine markers of immune activation namely TGF beta.

End point type	Secondary

End point timeframe:

48, 96 and 144 weeks

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: ng/L				
arithmetic mean (standard deviation)				
Week 48 (n= 67, 66)	64.1 (± 4857.31)	-165 (± 2584.89)		
Week 96 (n= 67, 66)	-227.5 (± 4417.59)	-296.5 (± 2200.97)		
Week 144 (n= 67, 66)	792 (± 6772.41)	1275.4 (± 5044.79)		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 48

Statistical analysis description:

The above analysis is for TGF-beta cells at Week 48. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3786
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	498.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-617.33
upper limit	1613.41

Statistical analysis title	Statistical analysis at Week 96

Statistical analysis description:

The above analysis is for TGF-beta cells at Week 96. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4388
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	348.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-539.61
upper limit	1237.01

Statistical analysis title	Statistical analysis at Week 144

Statistical analysis description:

The above analysis is for TGF-beta cells at Week 144. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8559
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-173.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2060.81
upper limit	1713.68

Secondary: Mean change from baseline in Log10 plasma Hepatitis C virus (HCV) RNA at Week 48, 96 and 144

End point title	Mean change from baseline in Log10 plasma Hepatitis C virus (HCV) RNA at Week 48, 96 and 144

End point description:

Plasma samples were used to determine HCV RNA using the Roche COBAS Ampliprep/COBAS HCV Taqman assay, RUO version (LOD=15 IU/mL).Baseline value for HCV RNA/HBV DNA is defined as the pre-dose measurement taken at Day 1 visit.

End point type	Secondary

End point timeframe:

48, 96 and 144 weeks

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: Log10 values				
arithmetic mean (standard deviation)				
Week 48 (n= 45, 45)	-3.2 (± 0.6)	-3.2 (± 0.68)		
Week 96 (n= 45, 45)	-3.2 (± 0.5)	-3.4 (± 0.81)		
Week 144 (n= 45, 45)	-3.1 (± 0.57)	-3.3 (± 0.72)		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 48

Statistical analysis description:

The above analysis is change for baseline in Log10 plasma HCV RNA at 48 Weeks. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8024
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	0.28

Statistical analysis title	Statistical analysis at Week 96

Statistical analysis description:

The above analysis is change for baseline in Log10 plasma HCV RNA at 96 Weeks. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo

Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.266
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.43

Statistical analysis title	Statistical analysis at Week 144

Statistical analysis description:

The above analysis is change for baseline in Log10 plasma HCV RNA at 144 Weeks. Results are from an ANCOVA model with change from baseline as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2855
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.41

Secondary: Mean change from baseline in plasma Hepatitis B virus (HBV) DNA at Week 48, 96 and 144

End point title	Mean change from baseline in plasma Hepatitis B virus (HBV) DNA at Week 48, 96 and 144

End point description:

Plasma samples were used to determine HBV DNA using the Roche COBAS TaqMan HBV assay. Baseline value for HCV RNA/HBV DNA is defined as the pre-dose measurement taken at Day 1 visit.

End point type	Secondary

End point timeframe:

48, 96 and 144 weeks

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: Log10 values				
arithmetic mean (standard deviation)				
Week 48 (n= 15, 10)	-2.6 (± 1.55)	-3 (± 0.11)		
Week 96 (n= 15, 14)	-3.3 (± 0.94)	-3 (± 0)		
Week 144 (n= 15, 15)	-3.4 (± 0.96)	-3 (± 0)		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 48

Statistical analysis description:

Results are from an ANCOVA model with change from baseline at Week 48 as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7778 [5]
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	1.23

Notes:

[5] - Not specified.

Statistical analysis title	Statistical analysis at Week 96

Statistical analysis description:

Results are from an ANCOVA model with change from baseline at Week 96 as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9991
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.1

Statistical analysis title	Statistical analysis at Week 144

Statistical analysis description:

Results are from an ANCOVA model with change from baseline at Week 144 as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7275
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.11

Secondary: Mean change from baseline in Enhanced Liver Fibrosis (ELF) test at Week 48, 96 and 144

End point title	Mean change from baseline in Enhanced Liver Fibrosis (ELF) test at Week 48, 96 and 144

End point description:

The markers of fibrosis assessed in this test comprised hyaluronic acid (CHA), tissue inhibitor of metalloproteinase (CTIMP1) and procollagen III N-terminal peptide (CP3NP); these are components of the extracellular matrix and basement sinusoidal membrane of the liver and are elevated during activation of the stellate cell. The ELF tests were performed on an ADVIA Centaur XP and the composite score was calculated as follows: ELF score = 2.278 + 0.851 ln(CHA) + 0.751 ln (CP3NP) + 0.394 ln(CTIMP1). ELF score < 7.7: no to mild fibrosis; ≥ 7.7 — < 9.8: Moderate fibrosis; ≥ 9.8 — < 11.3: Severe fibrosis; ≥ 11.3: Cirrhosis.

End point type	Secondary

End point timeframe:

48, 96 and 144 weeks

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: ELF score				
arithmetic mean (standard deviation)				
Week 48 (n= 70, 67)	0.2 (± 0.7)	0.1 (± 0.71)		
Week 96 (n= 70, 67)	0.4 (± 0.73)	0.4 (± 0.58)		
Week 144 (n= 70, 67)	0.4 (± 0.72)	0.4 (± 0.69)		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 48

Statistical analysis description:

Results are from an ANCOVA model with change from baseline at Week 48 as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5201 [6]
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.3

Notes:

[6] - Not specified.

Statistical analysis title	Statistical analysis at Week 96

Statistical analysis description:

Results are from an ANCOVA model with change from baseline at Week 96 as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4657
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.13

Statistical analysis title	Statistical analysis at Week 144

Statistical analysis description:

Results are from an ANCOVA model with change from baseline at Week 144 as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8087
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.2

Secondary: Mean change from baseline in the hepatic elastography (FibroscanTM) at Week 48, 96 and 144

End point title	Mean change from baseline in the hepatic elastography (FibroscanTM) at Week 48, 96 and 144

End point description:

Participants had transient hepatic elastography using FibroScan technology. It rapidly and non invasively measures hepatic tissue stiffness. Through a probe, a low frequency vibration of low amplitude is transmitted to the liver. The velocity of the wave that is generated during the procedure correlates directly with tissue stiffness as it passes through the liver; the harder or stiffer the liver, the faster the shear wave propagates. Results are reported in kilopascals (kPa). A negative change in the fibroscan values (i.e. decrease in liver stiffness) correlates with a decrease in fibrosis and thus improved outcome.

End point type	Secondary

End point timeframe:

48, 96 and 144 weeks

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	28		
Units: kPa				
arithmetic mean (standard deviation)				
Week 48 (n= 25, 28)	-1.3 (± 2.41)	0.4 (± 5.71)		
Week 96 (n= 25, 28)	-0.8 (± 2.95)	0.4 (± 5.7)		
Week 144 (n= 25, 28)	-1.7 (± 2.45)	-0.3 (± 4.39)		

Statistical analyses

Statistical analysis title	Statistical analysis at Week 48

Statistical analysis description:

Results are from an ANCOVA model with change from baseline at Week 48 as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1417 [7]
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.31
upper limit	0.63

Notes:

[7] - Not specified.

Statistical analysis title	Statistical analysis at Week 96

Statistical analysis description:

Results are from an ANCOVA model with change from baseline at Week 96 as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2679
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.01
upper limit	1.14

Statistical analysis title	Statistical analysis at Week 144

Statistical analysis description:

Results are from an ANCOVA model with change from baseline at Week 144 as the response variable and the following fixed effect model terms: treatment (Maraviroc or placebo), baseline value of the response variable, HBV, PI-based regimen.

Comparison groups	Maraviroc v Placebo

Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1366
Method	ANCOVA
Parameter estimate	Difference in LS Mean
Point estimate	-1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.45
upper limit	0.49

Secondary: Mean change from baseline in fibrosis score (Ishak) in liver biopsy samples at Week 144

End point title	Mean change from baseline in fibrosis score (Ishak) in liver biopsy samples at Week 144

End point description:

Samples were processed and sent to a central reader for scoring for fibrosis and other analyses such as Sirius red and α smooth muscle actin staining for activated stellate cells. Samples were collected, processed, stored and shipped in accordance with the procedure documented in a separate handling document. The Ishak fibrosis scoring system was used to score the fibrosis observed. The scores for liver biopsies were summarized based upon the availability of liver biopsy results.

End point type	Secondary

End point timeframe:

Week 144

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: Numerical score				
median (full range (min-max))	0 (-2 to 1)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants Who were Hospitalized Due to Hepatic Disease Through Week 144

End point title	Percentage of participants Who were Hospitalized Due to Hepatic Disease Through Week 144

End point description:

Healthcare resource utilization data was collected using the Healthcare Resource Utilization Questionnaire at all study visits except Screening and Baseline. Other components of healthcare resource utilization, including length of hospital stay, type of ward, associated investigative and therapeutic procedures and concomitant medications were captured from primary and secondary data sources.

End point type	Secondary
End point timeframe: 144 Weeks	

End point values	Maraviroc	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	67		
Units: Percentage of participants				
number (not applicable)				
Not Hospitalized	71.4	70.1		
Hospitalized due to Hepatic Disease at least once	10	5		
Hospitalized, but not due to Hepatic Disease	95	95		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Estimated Maraviroc PK Parameters

End point title	Summary of Estimated Maraviroc PK Parameters
End point description: Week 4 and Week 48 clinic visits were scheduled such that a trough sample may be taken within a time window of 8-16 hours after the previous dose (C trough). Blood samples (4 mL) were collected from all participants at the Week 4 and 48 visits.	
End point type	Secondary
End point timeframe: Week 48	

End point values	Maraviroc 150 mg	Maraviroc 300 mg	Maraviroc 600 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	31	8	28	
Units: ng/mL				
median (full range (min-max))				
Cavg	262 (35 to 455)	166 (72 to 187)	309 (79 to 656)	
Cmax	496 (47 to 768)	258 (162 to 528)	915 (133 to 1734)	
Cmin	127.2 (21.6 to 280.5)	61.3 (19.5 to 112.9)	69.2 (17.3 to 250.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Exposure-response relationship between change from baseline in liver fibrosis biomarkers versus MVC Cavg at Week 48

End point title	Exposure-response relationship between change from baseline in liver fibrosis biomarkers versus MVC Cavg at Week 48

End point description:

There was no apparent relationship between change from baseline in AST, ALT, BIL and ELF versus MVC Cavg. There was an apparent trend of greater decrease in FSCN and ALK from baseline with increasing MVC Cavg.

End point type	Secondary

End point timeframe:

Week 48

End point values	Aspartate transaminase (AST)	Alanine transaminase (ALT)	Bilirubin (BIL)	Enhanced Liver Fibrosis (ELF)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	67	67	67	67
Units: Units on a scale				
number (not applicable)				
p-value	0.892	0.44	0.766	0.795

End point values	Fibroscan (FSCN)	Alkaline phosphatase (ALK)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	67		
Units: Units on a scale				
number (not applicable)				
p-value	0.087	0.071		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of signing informed consent form up to 30 days after last dose of the study drug.

Adverse event reporting additional description:

The same event may appear as both an adverse event (AE) and a serious adverse event (SAE). However, what were presented were distinct events. An event may be categorized as serious in one participant and as nonserious in another participant, or one participant may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants who received placebo in combination with HAART

Reporting group title	Maraviroc

Reporting group description:

Participants who received maraviroc in combination with HAART

Serious adverse events	Placebo	Maraviroc	
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 67 (28.36%)	22 / 70 (31.43%)	
number of deaths (all causes)	2	3	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatic cancer			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Arthrodesis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Breast calcifications			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibrocystic breast disease			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiogenic pulmonary oedema			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Pyschotic disorder			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

Alanine aminotransferase increased			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose increased			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Foot fracture			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural hypotension			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic haematoma			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Syncope			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Seizure			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			

subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract nuclear			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			

Cushingoid			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal insufficiency			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Femoroacetabular impingement			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	3 / 70 (4.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia necrotising			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycobacterium avium complex infection			

subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	Maraviroc	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	62 / 67 (92.54%)	63 / 70 (90.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Skin papilloma			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Lipoma			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Oral papilloma			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	0	
Vascular disorders			
Haematoma			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hot flush			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Hypertension			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 67 (4.48%)	4 / 70 (5.71%)	
occurrences (all)	4	4	
Hypotension			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	

Varicose vein			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Deep vein thrombosis			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Peripheral venous disease			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Surgical and medical procedures			
Abdominal hernia repair			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Skin lesion excision			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Tooth extraction			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Cataract operation			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			

subjects affected / exposed	3 / 67 (4.48%)	1 / 70 (1.43%)	
occurrences (all)	4	1	
Axillary pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	4	0	
Chest pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 67 (4.48%)	3 / 70 (4.29%)	
occurrences (all)	4	3	
Chills			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Facial pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Fatigue			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 67 (4.48%)	5 / 70 (7.14%)	
occurrences (all)	3	5	
Feeling abnormal			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Influenza like illness			
alternative dictionary used: MedDRA 16.0			

alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	3 / 70 (4.29%)	
occurrences (all)	1	3	
Malaise			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Mucosal inflammation			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Nodule			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	3	0	
Oedema peripheral			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 67 (4.48%)	2 / 70 (2.86%)	
occurrences (all)	3	2	
Pyrexia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	4 / 70 (5.71%)	
occurrences (all)	2	4	
Chest discomfort			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Inflammation			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	

Pain			
subjects affected / exposed	1 / 67 (1.49%)	2 / 70 (2.86%)	
occurrences (all)	1	2	
Peripheral swelling			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Temperature intolerance			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Seasonal allergy			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	3 / 70 (4.29%)	
occurrences (all)	0	3	
Social circumstances			
Menopause			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Breast mass			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Genital rash			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Erectile dysfunction			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	

Prostatitis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Pruritus genital			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Testicular pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Genital lesion			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Gynaecomastia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Prostatic disorder			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal pruritus			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal swelling			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Cough			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	9 / 70 (12.86%)	
occurrences (all)	3	11	
Dyspnoea			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	1 / 70 (1.43%)	
occurrences (all)	2	2	
Haemoptysis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	4 / 70 (5.71%)	
occurrences (all)	3	5	
Productive cough			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Pharyngeal erythema			
alternative dictionary used: MedDRA 16.0			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Sinus congestion			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Sneezing			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Bronchial hyperreactivity			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Dry throat			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Pulmonary hypertension			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Pulmonary mass			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Sinus disorder			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	

Throat irritation			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Abnormal dreams			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Anxiety			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 67 (5.97%)	0 / 70 (0.00%)	
occurrences (all)	5	0	
Depression			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 67 (5.97%)	5 / 70 (7.14%)	
occurrences (all)	4	6	
Dissociation			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Nightmare			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Insomnia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 67 (8.96%)	5 / 70 (7.14%)	
occurrences (all)	6	5	

Sleep disorder alternative dictionary used: MedDRA 16.0 alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Alcohol abuse			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Alcoholism			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hallucination, auditory			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Paranoia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Substance abuse			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Suicidal ideation			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased alternative dictionary used: MedDRA 16.0 alternative assessment type: Systematic			
subjects affected / exposed	4 / 67 (5.97%)	1 / 70 (1.43%)	
occurrences (all)	4	1	
Aspartate aminotransferase increased alternative dictionary used: MedDRA 16.0 alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Blood creatinine increased			

alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Blood pressure increased			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Intraocular pressure increased			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Transaminases increased			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Lipase increased			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 67 (4.48%)	0 / 70 (0.00%)	
occurrences (all)	3	0	
Viral load increased			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Amylase increased			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Hepatic enzyme increased			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Liver function test abnormal			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	4 / 67 (5.97%)	1 / 70 (1.43%)	
occurrences (all)	5	1	
Anal pap smear abnormal			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Arthropod sting			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Contusion			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	2 / 70 (2.86%)	
occurrences (all)	3	2	
Exposure to communicable disease			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Fibula fracture			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Joint injury			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hand fracture			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Laceration			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 67 (4.48%)	1 / 70 (1.43%)	
occurrences (all)	3	1	
Ligament sprain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	2 / 70 (2.86%)	
occurrences (all)	2	2	
Limb injury			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Muscle strain			
alternative dictionary used: MedDRA 16.0			

alternative assessment type: Systematic			
subjects affected / exposed	3 / 67 (4.48%)	0 / 70 (0.00%)	
occurrences (all)	3	0	
Procedural pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Radius fracture			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Spinal compression fracture			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Bone contusion			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Epicondylitis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Humerus fracture			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Lower limb fracture			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Muscle injury			

subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Overdose			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal injury			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Wound			
subjects affected / exposed	0 / 67 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Cardiac disorders			
Angina pectoris			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Supraventricular tachycardia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Tachycardia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Nervous system disorders			
Ageusia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Amnesia			
alternative dictionary used: MedDRA 16.0			

alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Burning sensation			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Carpal tunnel syndrome			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Complex regional pain syndrome			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Cervicobrachial syndrome			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Dizziness			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 67 (8.96%)	4 / 70 (5.71%)	
occurrences (all)	7	4	
Dysaesthesia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Dysgeusia			

alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)		
occurrences (all)	1	0		
Headache				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	5 / 67 (7.46%)	6 / 70 (8.57%)		
occurrences (all)	7	7		
Hypertonia				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)		
occurrences (all)	0	2		
Hypoaesthesia				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)		
occurrences (all)	1	1		
Migraine				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 67 (4.48%)	3 / 70 (4.29%)		
occurrences (all)	5	4		
Intercostal neuralgia				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)		
occurrences (all)	0	1		
Sciatica				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				

subjects affected / exposed	2 / 67 (2.99%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Somnolence			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Aphasia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Disturbance in attention			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Dyskinesia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Epilepsy			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Hemiparesis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Loss of consciousness			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
VIIth nerve paralysis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 67 (1.49%)	2 / 70 (2.86%)	
occurrences (all)	1	2	
Lymphadenopathy			

subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	2	
Ear and labyrinth disorders			
Deafness			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Ear pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Tinnitus			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Vertigo			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 67 (4.48%)	2 / 70 (2.86%)	
occurrences (all)	3	2	
Vertigo positional			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Hearing impaired			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	

Hypoacusis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Arteriosclerotic retinopathy			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Chalazion			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Conjunctival hyperaemia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Eye swelling			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Retinopathy			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Blepharitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Eye disorder			

subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Retinopathy hypertensive			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Endocrine ophthalmopathy			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Glaucoma			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Abdominal pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 67 (5.97%)	1 / 70 (1.43%)	
occurrences (all)	4	1	
Abdominal pain upper			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Anal fissure			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Anal haemorrhage			
alternative dictionary used: MedDRA 16.0			
alternative assessment type:			

Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Constipation			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Diarrhoea			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 67 (17.91%)	8 / 70 (11.43%)	
occurrences (all)	14	11	
Dry mouth			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Dyspepsia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Faecaloma			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Flatulence			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Gastritis			

alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 67 (4.48%)	0 / 70 (0.00%)		
occurrences (all)	4	0		
Gastrointestinal disorder				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)		
occurrences (all)	1	0		
Gastrooesophageal reflux disease				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)		
occurrences (all)	1	1		
Haemorrhoids				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 67 (1.49%)	3 / 70 (4.29%)		
occurrences (all)	1	3		
Hiatus hernia				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)		
occurrences (all)	1	0		
Nausea				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	9 / 67 (13.43%)	7 / 70 (10.00%)		
occurrences (all)	10	7		
Proctitis				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)		
occurrences (all)	1	0		
Tongue disorder				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)		
occurrences (all)	0	1		
Tooth loss				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)		
occurrences (all)	1	0		
Toothache				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	7 / 67 (10.45%)	1 / 70 (1.43%)		
occurrences (all)	8	2		
Vomiting				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	7 / 67 (10.45%)	5 / 70 (7.14%)		
occurrences (all)	8	6		
Abdominal distension				
subjects affected / exposed	3 / 67 (4.48%)	1 / 70 (1.43%)		
occurrences (all)	3	1		
Abdominal symptom				
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)		
occurrences (all)	0	1		
Abdominal tenderness				
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)		
occurrences (all)	0	1		
Anorectal discomfort				
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)		
occurrences (all)	1	0		

Duodenogastric reflux			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Erosive oesophagitis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Food poisoning			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Gingival bleeding			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Gingival swelling			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Umbilical hernia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Cholestasis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hepatic pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hepatomegaly			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Hyperbilirubinaemia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hypertransaminasaemia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Liver disorder			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Hepatic steatosis			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Acne			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Alopecia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Dermatitis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 67 (1.49%)	2 / 70 (2.86%)	
occurrences (all)	1	2	
Hyperhidrosis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Night sweats			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	3 / 70 (4.29%)	
occurrences (all)	1	3	
Pruritus			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 67 (8.96%)	4 / 70 (5.71%)	
occurrences (all)	6	5	
Rash			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 67 (4.48%)	5 / 70 (7.14%)	
occurrences (all)	5	5	
Rash maculo-papular			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Rosacea			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Seborrhoeic dermatitis			
alternative dictionary used: MedDRA 16.0			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Skin lesion			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 67 (4.48%)	2 / 70 (2.86%)	
occurrences (all)	5	2	
Skin mass			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Actinic keratosis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Dermatitis allergic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	2	
Dermatitis contact			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Dyshidrotic eczema			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Eczema			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Onycholysis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Erythema			

subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Rash papular			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Skin fissures			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Skin plaque			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Skin ulcer			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Spider naevus			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Swelling face			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Rash pruritic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Dysuria			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	2 / 70 (2.86%)	
occurrences (all)	2	2	
Leukocyturia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Haematuria			

alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Micturition urgency			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Nephrolithiasis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Renal cyst			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Urinary hesitation			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	2	
Bladder prolapse			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Polyuria			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Urethral discharge			

subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Urinary incontinence			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Basedow's disease			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hypogonadism			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hypothyroidism			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 67 (8.96%)	7 / 70 (10.00%)	
occurrences (all)	7	8	
Back pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 67 (14.93%)	4 / 70 (5.71%)	
occurrences (all)	12	7	
Bursitis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 67 (4.48%)	0 / 70 (0.00%)	
occurrences (all)	3	0	
Flank pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Intervertebral disc protrusion			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Joint effusion			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Muscular weakness			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Musculoskeletal chest pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal pain			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 67 (5.97%)	0 / 70 (0.00%)	
occurrences (all)	4	0	
Musculoskeletal stiffness			
alternative dictionary used: MedDRA 16.0			

alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Myalgia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	2 / 70 (2.86%)	
occurrences (all)	2	2	
Pain in extremity			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 67 (10.45%)	3 / 70 (4.29%)	
occurrences (all)	9	3	
Pain in jaw			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Rotator cuff syndrome			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Spinal osteoarthritis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Arthritis			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Costochondritis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	

Gouty arthritis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	2	
Intervertebral disc disorder			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Musculoskeletal discomfort			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Osteopenia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Spondylitis			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Abscess neck			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Acarodermatitis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Acute tonsillitis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Bronchitis			

alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	7 / 67 (10.45%)	10 / 70 (14.29%)		
occurrences (all)	11	13		
Cellulitis				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)		
occurrences (all)	2	1		
Chlamydial infection				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)		
occurrences (all)	0	2		
Folliculitis				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)		
occurrences (all)	1	1		
Gastritis viral				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)		
occurrences (all)	0	1		
Gastroenteritis				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 67 (1.49%)	4 / 70 (5.71%)		
occurrences (all)	1	6		
Gingival abscess				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Herpes simplex			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	3 / 70 (4.29%)	
occurrences (all)	4	4	
Infection			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	2	
Laryngitis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Latent tuberculosis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Nasopharyngitis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 67 (8.96%)	9 / 70 (12.86%)	
occurrences (all)	11	16	
Onychomycosis			
alternative dictionary used: MedDRA 16.0			

alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Oral candidiasis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	3	
Oral herpes			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	2 / 70 (2.86%)	
occurrences (all)	1	2	
Oral infection			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Otitis externa			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	1 / 70 (1.43%)	
occurrences (all)	2	2	
Otitis media			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	3 / 70 (4.29%)	
occurrences (all)	0	3	
Otitis media fungal			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Penile abscess			

alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)		
occurrences (all)	0	1		
Pharyngitis				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 67 (2.99%)	5 / 70 (7.14%)		
occurrences (all)	3	6		
Pneumonia				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	5 / 67 (7.46%)	0 / 70 (0.00%)		
occurrences (all)	5	0		
Rash pustular				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)		
occurrences (all)	0	1		
Respiratory tract infection				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	4 / 67 (5.97%)	2 / 70 (2.86%)		
occurrences (all)	4	3		
Rhinitis				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 67 (0.00%)	2 / 70 (2.86%)		
occurrences (all)	0	2		
Schistosomiasis				
alternative dictionary used: MedDRA 16.0				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Secondary syphilis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 67 (5.97%)	5 / 70 (7.14%)	
occurrences (all)	4	5	
Subcutaneous abscess			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 67 (4.48%)	2 / 70 (2.86%)	
occurrences (all)	4	2	
Syphilis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 67 (11.94%)	3 / 70 (4.29%)	
occurrences (all)	8	4	
Tinea infection			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Tonsillitis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Tooth abscess			
alternative dictionary used: MedDRA 16.0			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	3 / 70 (4.29%)	
occurrences (all)	0	3	
Tooth infection			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	4 / 70 (5.71%)	
occurrences (all)	1	4	
Upper respiratory tract infection			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 67 (16.42%)	11 / 70 (15.71%)	
occurrences (all)	15	15	
Urethritis			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Urinary tract infection			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 67 (7.46%)	3 / 70 (4.29%)	
occurrences (all)	5	6	
Viral infection			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 67 (5.97%)	6 / 70 (8.57%)	
occurrences (all)	5	8	
Acute sinusitis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Carbuncle			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	

Body tinea			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Chikungunya virus infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Ear infection			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Fungal skin infection			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Furuncle			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Gastroenteritis viral			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Genital herpes simplex			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Gingivitis			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Groin abscess			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Herpes virus infection			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	3 / 67 (4.48%)	1 / 70 (1.43%)	
occurrences (all)	3	1	

Lower respiratory tract infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Mastitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Muscle abscess			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Oesophageal candidiasis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Post procedural infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Proctitis chlamydial			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Streptococcal infection			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Epididymitis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 67 (4.48%)	0 / 70 (0.00%)	
occurrences (all)	4	0	
Dyslipidaemia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Gout			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 67 (2.99%)	0 / 70 (0.00%)	
occurrences (all)	3	0	
Hypercholesterolaemia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Hypertriglyceridaemia			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 67 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Obesity			
alternative dictionary used: MedDRA 16.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Hypophosphataemia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Vitamin D deficiency			
subjects affected / exposed	3 / 67 (4.48%)	2 / 70 (2.86%)	
occurrences (all)	3	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 October 2011	The text regarding acceptable methods of contraception was revised.Exemption to restart study drug was clarified. HIV viral suppression prior to screening and for randomization, power of the study were clarified. The participants receiving drugs known to elevate total bilirubin were not regarded as Hy's Law cases. Section 4.3.1 regarding contraception, Section 6.6 regarding subject withdrawal and Section 8.9 regarding exposure during pregnancy were updated. The details of ViiV Healthcare (Sponsor) were added. AIDS Clinical Trials Group (ACTG) Severity Grading Table in Appendix 5 with current division of AIDS (DAIDS) Severity Table and corresponding text were replaced.
25 June 2012	The safety text in relevant Adverse Event Reporting sections was updated. Revised the single reference safety document (SRSD) is the Investigator's Brochure (IB). The pregnancy testing was added in Section 7. Revised Section 8.7 Severity Assessment to align with the DAIDS grading table.
12 December 2013	The investigator, site staff, participant and blinded assessor unblinding details in the protocol summary study design and sections 3.1 and 5.2 were updated. Updated section 4.2 to align exclusion criteria 21 with current template text. Added section 4.4 to align with the updated Sponsor protocol template clarifying access to Sponsor qualified medical personnel. Updated section 5.3.4 to further clarify lack of compliance consideration. Updated section 6.5 to clarify requirements for participants being followed In Study Off-Drug ("ISOD"). Updated section 7.7.3 to clarify blood samples may only be analysed for markers of liver fibrosis in the blood. Updated section 8.2 to clarify all SAEs must be reported following the active reporting period has ended. Added section 8.5.1 to align with the updated Sponsor protocol template and confirm there were no protocol-specific SAEs defined for the study. Updated section 8.7 DAIDs Appendix reference from Appendix 5 to Appendix 2. Section 15 was updated to remove reference from the Clinical Study Agreement and further confirm Sponsor practices for posting basic reuslts.

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.

The median time to development of Grade 3 and Grade 4 ALT abnormalities was not estimable as few events reported under each treatment group.

Notes: