Clinical trial results:
PROTEAse inhibitor (DRV/rtv) in mono- or triple therapy in suppressed HIV-1 infected subjects

Summary

EudraCT number	2011-001635-23
Trial protocol	BE GB IE DE ES AT HU DK IT SE PL
Global end of trial date	18 March 2015

Results information

Result version number	v1 (current)
This version publication date	09 March 2016
First version publication date	09 March 2016

Trial information

Trial identification

Sponsor protocol code	TMC114IFD3003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01448707
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Cilag International N.V.
Sponsor organisation address	Turnhoutseweg 30, Beerse, Belgium, 2340
Public contact	Clinical Registry Group , Janssen Cilag International N.V., ClinicaltrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group , Janssen Cilag International N.V., ClinicaltrialsEU@its.jnj.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	25 June 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to demonstrate the non-inferiority in terms of the percentage of participants who have plasma human immunodeficiency type 1 (HIV-1) ribonucleic acid (RNA) levels less than (<) 50 copies/milliliters (mL) after 48 weeks of follow-up after switching to darunavir/ritonavir (DRV/rtv) monotherapy versus triple therapy containing DRV/rtv along with 2 nucleoside analogues [Food and Drug Administration (FDA) Snapshot method].

Protection of trial subjects:

Safety evaluations for this study included the monitoring of adverse events (AEs); laboratory tests (hematology, biochemistry, urinalysis, serum pregnancy test and hepatitis serology); vital sign measurements and physical examinations. An Independent data monitoring committee was involved for the safety evaluation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 January 2012
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	Austria: 10
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Denmark: 15
Country: Number of subjects enrolled	France: 28
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Ireland: 8
Country: Number of subjects enrolled	Israel: 10
Country: Number of subjects enrolled	Italy: 46
Country: Number of subjects enrolled	Poland: 13
Country: Number of subjects enrolled	Spain: 40
Country: Number of subjects enrolled	Sweden: 7
Country: Number of subjects enrolled	Switzerland: 15
Country: Number of subjects enrolled	United Kingdom: 36
Worldwide total number of subjects	273
EEA total number of subjects	248

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)	261
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

274 participants were randomized in to the study treatment with 1:1 ratio. One randomized participant was not treated.

Pre-assignment

Screening details:

The study consisted of a screening period up to 6 weeks, a 4-week run-in phase (Baseline 1), and a 96 week treatment period (which starts at Baseline 2), followed by a 30- to 35-day follow-up period.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	DRV/rtv MONO

Arm description:

Participants received 2 tablets of Darunavir (DRV) 400 milligram (mg) and 1 tablet of ritonavir (rtv) 100 mg within 30 minutes after a meal.

Arm type	Experimental
Investigational medicinal product name	Darunavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets of DRV 400 mg within 30 minutes after a meal.

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 1 tablet of rtv 100 mg within 30 minutes after a meal.

Arm title	DRV/rtv + 2NRTIs

Arm description:

Participants received 2 tablets of DRV 400 mg and 1 tablet of rtv 100 mg within 30 minutes after a meal in combination with 2 nucleoside reverse transcriptase inhibitor (N[t]RTIs), an investigator-selected dual combination of either abacavir (ABC), lamivudine (3TC), zidovudine (AZT), tenofovir disoproxil fumarate (TDF) or emtricitabine (FTC).

Arm type	Experimental
Investigational medicinal product name	Darunavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets of DRV 400 mg within 30 minutes after a meal in combination with 2 N[t]RTIs.

Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 1 tablet of rtv 100 mg within 30 minutes after a meal in combination with 2 N[t]RTIs.

Investigational medicinal product name	Abacavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets of DRV 400 mg and 1 tablet of rtv 100 mg within 30 minutes after a meal in combination with abacavir.

Investigational medicinal product name	lamivudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets of DRV 400 mg and 1 tablet of rtv 100 mg within 30 minutes after a meal in combination with lamivudine.

Investigational medicinal product name	Zidovudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets of DRV 400 mg and 1 tablet of rtv 100 mg within 30 minutes after a meal in combination with zidovudine.

Investigational medicinal product name	Tenofovir Disoproxil Fumarate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets of DRV 400 mg and 1 tablet of rtv 100 mg within 30 minutes after a meal in combination with tenofovir disoproxil fumarate.

Investigational medicinal product name	Emtricitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 tablets of DRV 400 mg and 1 tablet of rtv 100 mg within 30 minutes after a meal in combination with emtricitabine.

Number of subjects in period 1	DRV/rtv MONO	DRV/rtv + 2NRTIs
Started	137	136
Completed	119	118
Not completed	18	18
Adverse Event	3	1
Withdrawal By Subject	6	7
Other	7	4
Lost to follow-up	2	6

Baseline characteristics

Reporting groups	
Reporting group title	DRV/rtv MONO
Reporting group description:	
Participants received 2 tablets of Darunavir (DRV) 400 milligram (mg) and 1 tablet of ritonavir (rtv) 100 mg within 30 minutes after a meal.	
Reporting group title	DRV/rtv + 2NRTIs
Reporting group description:	
Participants received 2 tablets of DRV 400 mg and 1 tablet of rtv 100 mg within 30 minutes after a meal in combination with 2 nucleoside reverse transcriptase inhibitor (N[t]RTIs), an investigator-selected dual combination of either abacavir (ABC), lamivudine (3TC), zidovudine (AZT), tenofovir disoproxil fumarate (TDF) or emtricitabine (FTC).	

Reporting group values	DRV/rtv MONO	DRV/rtv + 2NRTIs	Total
Number of subjects	137	136	273
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	131	130	261
From 65 to 84 years	6	6	12
85 years and over	0	0	0
Title for AgeContinuous			
Units: years			
arithmetic mean	44.6	43.1	
standard deviation	± 11.21	± 10.41	-
Title for Gender			
Units: subjects			
Female	26	21	47
Male	111	115	226

End points

End points reporting groups

Reporting group title	DRV/rtv MONO

Reporting group description:

Participants received 2 tablets of Darunavir (DRV) 400 milligram (mg) and 1 tablet of ritonavir (rtv) 100 mg within 30 minutes after a meal.

Reporting group title	DRV/rtv + 2NRTIs

Reporting group description:

Participants received 2 tablets of DRV 400 mg and 1 tablet of rtv 100 mg within 30 minutes after a meal in combination with 2 nucleoside reverse transcriptase inhibitor (N[t]RTIs), an investigator-selected dual combination of either abacavir (ABC), lamivudine (3TC), zidovudine (AZT), tenofovir disoproxil fumarate (TDF) or emtricitabine (FTC).

Subject analysis set title	DRV/rtv MONO
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intention-to-treat (ITT) analysis set included all participants who were randomized and who took at least one dose of study medication in the Treatment phase, regardless of their compliance with the protocol.

Subject analysis set title	DRV/rtv + 2NRTIs
Subject analysis set type	Intention-to-treat

Subject analysis set description:

ITT analysis set included all participants who were randomized and who took at least one dose of study medication in the Treatment phase, regardless of their compliance with the protocol.

Primary: Virologic Response (Food drug and administration [FDA] Snapshot, Switch = Failure)

End point title	Virologic Response (Food drug and administration [FDA] Snapshot, Switch = Failure)

End point description:

The percentage of participants who have plasma human immunodeficiency virus type-1 (HIV-1) ribonucleic acid (RNA) levels less than (<) 50 copies/milliliters [mL] after 48 weeks of follow-up after switching to DRV/ritonavir (rtv) monotherapy versus triple therapy containing DRV/rtv.

End point type	Primary

End point timeframe:

Week 48

End point values	DRV/rtv MONO	DRV/rtv + 2NRTIs		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	137[1]	136[2]		
Units: percentage of participants				
number (not applicable)	87	95		

Notes:

[1] - ITT Population

[2] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	DRV/rtv + 2NRTIs v DRV/rtv MONO

Number of subjects included in analysis	273
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	= 0.2331
Method	Mixed models analysis
Parameter estimate	Non-Linear mixed model
Point estimate	-7.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.64
upper limit	-1.19

Notes:

[3] - Non-inferiority of DRV/rtv monotherapy versus triple therapy was assessed with a maximum allowable difference of 12 percent (%).

Secondary: Virologic Response (Food drug and administration [FDA] Snapshot, Switch = Failure)

End point title	Virologic Response (Food drug and administration [FDA] Snapshot, Switch = Failure)

End point description:

The percentage of participants who have plasma human immunodeficiency virus type-1 (HIV-1) ribonucleic acid (RNA) levels <50 copies/milliliters [mL] after 96 weeks of follow-up after switching to DRV/ritonavir (rtv) monotherapy versus triple therapy containing DRV/rtv.

End point type	Secondary

End point timeframe:

Week 96

End point values	DRV/rtv MONO	DRV/rtv + 2NRTIs		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	137[4]	136[5]		
Units: percentage of participants				
number (not applicable)	75.2	85.3		

Notes:

[4] - ITT Population

[5] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	DRV/rtv MONO v DRV/rtv + 2NRTIs
Number of subjects included in analysis	273
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
P-value	= 0.6933
Method	Mixed models analysis
Parameter estimate	Non-Linear mixed model
Point estimate	-10.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.5
upper limit	-0.73

Notes:

[6] - Non-inferiority of DRV/rtv monotherapy versus triple therapy was assessed with a maximum allowable difference of 12 percent (%).

Secondary: Virologic Response (FDA Snapshot, Switch included)

End point title	Virologic Response (FDA Snapshot, Switch included)

End point description:

The percentage of participants who have plasma human immunodeficiency virus type-1 (HIV-1) ribonucleic acid (RNA) levels <50 copies/mL after 48 and 96 weeks of follow-up after switching to DRV/ritonavir(rtv) monotherapy versus triple therapy containing DRV/rtv.

End point type	Secondary

End point timeframe:

Week 48 and 96

End point values	DRV/rtv MONO	DRV/rtv + 2NRTIs		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	137[7]	136[8]		
Units: percentage				
number (not applicable)				
Week 48	93	96.5		
Week 96	89.3	89.9		

Notes:

[7] - ITT Population

[8] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis Week 48
Comparison groups	DRV/rtv MONO v DRV/rtv + 2NRTIs
Number of subjects included in analysis	273
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
P-value	= 0.0016
Method	Mixed models analysis
Parameter estimate	non-linear mixed model
Point estimate	-3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.77
upper limit	1.72

Notes:

[9] - Week 48: Non-inferiority of DRV/rtv monotherapy versus triple therapy was assessed with a maximum allowable difference of 12 percent (%).

Statistical analysis title	Statistical Analysis Week 96
Comparison groups	DRV/rtv MONO v DRV/rtv + 2NRTIs
Number of subjects included in analysis	273
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
P-value	= 0.0022
Method	Mixed models analysis
Parameter estimate	Non-linear mixed model
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.89
upper limit	6.58

Notes:

[10] - Week 96: Non-inferiority of DRV/rtv monotherapy versus triple therapy was assessed with a maximum allowable difference of 12 percent (%).

Secondary: Change From Baseline in Global Neurocognitive Performance z Score

End point title	Change From Baseline in Global Neurocognitive Performance z Score

End point description:

Change in neurocognitive function of DRV/rtv monotherapy versus triple therapy containing DRV/rtv over 48 and 96 weeks. Neurocognitive function was measured by Hopkins Verbal Learning Test (verbal learning and memory), Colour Trail Test (psychomotor speed and cognitive flexibility) and Grooved Pegboard Test (psychomotor speed and fine motor function). Higher values for change in z-score represent an improvement in Neurocognitive Performance (NP).

End point type	Secondary

End point timeframe:

Baseline, Week 48 and 96

End point values	DRV/rtv MONO	DRV/rtv + 2NRTIs		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	137[11]	136[12]		
Units: units on a scale				
arithmetic mean (standard error)				
Change at Week 48	0.39 (± 0.048)	0.42 (± 0.057)		
Change at Week 96	0.63 (± 0.06)	0.57 (± 0.057)		

Notes:

[11] - ITT Population

[12] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Loss of Virologic Response

End point title	Time to Loss of Virologic Response

End point description:

Time to loss of virologic response (<50 copies/mL, FDA Snapshot switch = failure) measured over time.

Here 99999 signifies "Not Available (NA)", because the event occurred in less than 50 percent of the participants.

End point type	Secondary

End point timeframe:

Baseline up to Week 48 or early withdrawal

End point values	DRV/rtv MONO	DRV/rtv + 2NRTIs		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	137[13]	136[14]		
Units: days				
median (full range (min-max))	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[13] - ITT Population

[14] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Reporting Treatment-Emergent Phenotypic Drug Resistance

End point title	Number of Participants Reporting Treatment-Emergent Phenotypic Drug Resistance

End point description:

The loss of treatment options of DRV/rtv monotherapy versus triple therapy containing DRV/rtv at Weeks 48 and 96, as defined by treatment-emergent phenotypic drug resistance. Drug resistance is classified as: 1) Confirmed HIV RNA >= 400 copies/mL, 2) Post-baseline phenotypic data and 3) Phenotypic resistance to any of the drug classes (NRTI, NNRTI, or PI).

End point type	Secondary

End point timeframe:

At Weeks 48 and 96

End point values	DRV/rtv MONO	DRV/rtv + 2NRTIs		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	137[15]	136[16]		
Units: participants				
number (not applicable)				
Confirmed HIV RNA >= 400 copies/mL	1	2		
Post-baseline phenotypic data	2	1		
Phenotypic resistance to any of the drug classes	0	0		

Notes:

[15] - ITT Population

[16] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Reporting Resistance Mutations With Confirmed Virologic Failure Who Have HIV RNA >400 Copies/mL and Genotype Resistance Results

End point title	Number of Participants Reporting Resistance Mutations With Confirmed Virologic Failure Who Have HIV RNA >400 Copies/mL and Genotype Resistance Results

End point description:

The viral genotype of participants treated with DRV/rtv monotherapy versus triple therapy containing DRV/rtv over 48 and 96 weeks. Genotypic resistance (number of resistance mutations) at any time point when a participant had a confirmed plasma VL >400 copies/mL after randomization was performed per treatment group for the ITT population. Results were summarized based on individual treatment received: Darunavir resistance mutations, non-nucleoside reverse transcriptase inhibitor (NNRTI) mutations, nucleoside reverse transcriptase inhibitor (NRTI) mutations, protease inhibitor (PI) resistance mutations, PR mutations, RT mutations, extended NNRTI mutations, primary PI mutations.

End point type	Secondary

End point timeframe:

Over 48 and 96 Weeks

End point values	DRV/rtv MONO	DRV/rtv + 2NRTIs		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	137[17]	136[18]		
Units: participants				
number (not applicable)				
Participans with HIV RNA >= 400 copies/mL	1	2		
Number of 0 Darunavir resistance mutations	2	1		
Number of 0 NNRTI mutations	2	0		
Number of 1 NNRTI mutations	0	1		
Number of 1 PI resistance mutations	1	0		
Number of 5 PI resistance mutations	0	1		
Number of 6 PI resistance mutations	1	0		
Number of 11 PR mutations	0	1		
Number of 15 PR mutations	1	0		
Number of 7 PR mutations	1	0		
Number of 14 RT mutations	1	0		
Number of 16 RT mutations	0	1		
Number of 33 RT mutations	1	0		
Number of extended 0 NNRTI mutations	2	0		
Number of extended 1 NNRTI mutations	0	1		
Number of primary 0 PI mutations	2	1		
Number of participants with no mutations	0	0		

Notes:

[17] - ITT Population

[18] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to 96 weeks	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups	
Reporting group title	DRV/rtv MONO
Reporting group description:	
Participants received 2 tablets of Darunavir (DRV) 400 milligram (mg) and 1 tablet of ritonavir (rtv) 100 mg within 30 minutes after a meal.	
Reporting group title	DRV/rtv + 2NRTIs
Reporting group description:	
Participants received 2 tablets of DRV 400 mg and 1 tablet of rtv 100 mg within 30 minutes after a meal in combination with 2 nucleoside reverse transcriptase inhibitor (N[t]RTIs), an investigator-selected dual combination of either abacavir (ABC), lamivudine (3TC), zidovudine (AZT), tenofovir disoproxil fumarate (TDF) or emtricitabine (FTC).	

Serious adverse events	DRV/rtv MONO	DRV/rtv + 2NRTIs	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 137 (13.14%)	14 / 136 (10.29%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital Warts			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's Disease			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast Cancer			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse Large B-Cell Lymphoma			

subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Gastrectomy			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillectomy			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
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			
Pyrexia			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenderness			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Nasal Obstruction			

subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcoholism			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Substance Abuse			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
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			
Facial Bones Fracture			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal Injury			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar Vertebral Fracture			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Post Lumbar Puncture Syndrome			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius Fracture			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac Arrest			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (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			
Central Nervous System Lesion			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalomyelitis			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic Stroke			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			

subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic Neuritis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Anal Fistula			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Excessive Granulation Tissue			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Ulcer			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash Pruritic			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (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			
Renal Failure			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus Urinary			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Retention			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cytomegalovirus Infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Viral			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin Abscess			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis B			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis C			
subjects affected / exposed	2 / 137 (1.46%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis Bacterial			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shigella Infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (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			
Hyperkalaemia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	DRV/rtv MONO	DRV/rtv + 2NRTIs	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	110 / 137 (80.29%)	106 / 136 (77.94%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anal Neoplasm			
subjects affected / exposed	2 / 137 (1.46%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Anogenital Warts			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Basal Cell Carcinoma			
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)	
occurrences (all)	0	2	
Colon Adenoma			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Fibroma			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Gastrointestinal Neoplasm			

subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	2	
Lipoma			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	2	
Lymphoma			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Melanocytic Naevus			
subjects affected / exposed	2 / 137 (1.46%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Skin Papilloma			
subjects affected / exposed	2 / 137 (1.46%)	1 / 136 (0.74%)	
occurrences (all)	2	1	
Uterine Leiomyoma			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)	
occurrences (all)	0	2	
Hypertension			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	2	
Venous Thrombosis			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 137 (0.73%)	5 / 136 (3.68%)	
occurrences (all)	1	5	
Chest Discomfort			

subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Chest Pain			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Cyst			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Facial Pain			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	7 / 137 (5.11%)	7 / 136 (5.15%)	
occurrences (all)	7	7	
Influenza Like Illness			
subjects affected / exposed	6 / 137 (4.38%)	6 / 136 (4.41%)	
occurrences (all)	6	6	
Local Swelling			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Oedema Peripheral			
subjects affected / exposed	0 / 137 (0.00%)	3 / 136 (2.21%)	
occurrences (all)	0	3	
Pain			
subjects affected / exposed	4 / 137 (2.92%)	1 / 136 (0.74%)	
occurrences (all)	8	1	
Polyp			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Pyrexia			

subjects affected / exposed	4 / 137 (2.92%)	7 / 136 (5.15%)	
occurrences (all)	4	8	
Spinal Pain			
subjects affected / exposed	2 / 137 (1.46%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Swelling			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Tenderness			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	2	
Ulcer			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Balanitis			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Breast Mass			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Erectile Dysfunction			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Gynaecomastia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Metrorrhagia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Orchitis Noninfective			

subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Sexual Dysfunction			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Uterine Fibrosis			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Bronchial Hyperreactivity			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Bronchitis Chronic			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	8 / 137 (5.84%)	8 / 136 (5.88%)	
occurrences (all)	8	8	
Dyspnoea			
subjects affected / exposed	2 / 137 (1.46%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Dyspnoea Exertional			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Nasal Congestion			
subjects affected / exposed	2 / 137 (1.46%)	1 / 136 (0.74%)	
occurrences (all)	2	1	
Oropharyngeal Pain			
subjects affected / exposed	4 / 137 (2.92%)	2 / 136 (1.47%)	
occurrences (all)	4	2	
Respiratory Tract Irritation			

subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Rhinitis Allergic			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Sleep Apnoea Syndrome			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Tonsillar Hypertrophy			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Upper Respiratory Tract Inflammation			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Wheezing			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Psychiatric disorders			
Abnormal Behaviour			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Anhedonia			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	2 / 137 (1.46%)	3 / 136 (2.21%)	
occurrences (all)	3	3	
Borderline Personality Disorder			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Depressed Mood			

subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Depression			
subjects affected / exposed	4 / 137 (2.92%)	7 / 136 (5.15%)	
occurrences (all)	4	7	
Middle Insomnia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	6 / 137 (4.38%)	5 / 136 (3.68%)	
occurrences (all)	6	5	
Nervousness			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Nightmare			
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)	
occurrences (all)	0	2	
Panic Attack			
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)	
occurrences (all)	0	2	
Sleep Disorder			
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)	
occurrences (all)	0	2	
Stress			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Social Phobia			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Substance Abuse			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	2	1	

Amylase Increased				
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)		
occurrences (all)	2	0		
Aspartate Aminotransferase Increased				
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)		
occurrences (all)	0	1		
Blood Cholesterol Increased				
subjects affected / exposed	6 / 137 (4.38%)	2 / 136 (1.47%)		
occurrences (all)	7	2		
Blood Alkaline Phosphatase Increased				
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)		
occurrences (all)	0	1		
Blood Creatine Phosphokinase Increased				
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)		
occurrences (all)	1	0		
Blood Creatinine Increased				
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)		
occurrences (all)	1	1		
Blood Folate Decreased				
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)		
occurrences (all)	1	0		
Blood Potassium Decreased				
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)		
occurrences (all)	1	0		
Blood Thyroid Stimulating Hormone Increased				
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)		
occurrences (all)	1	0		
Blood Pressure Diastolic Increased				
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)		
occurrences (all)	1	0		
Body Temperature Increased				
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)		
occurrences (all)	1	0		
Bone Density Decreased				

subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)		
occurrences (all)	0	1		
C-Reactive Protein Increased				
subjects affected / exposed	0 / 137 (0.00%)	3 / 136 (2.21%)		
occurrences (all)	0	3		
Glomerular Filtration Rate Decreased				
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)		
occurrences (all)	1	0		
Haemoglobin Decreased				
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)		
occurrences (all)	0	2		
Hepatic Enzyme Increased				
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)		
occurrences (all)	1	1		
Lipase Increased				
subjects affected / exposed	2 / 137 (1.46%)	0 / 136 (0.00%)		
occurrences (all)	4	0		
Platelet Count Decreased				
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)		
occurrences (all)	0	2		
Prostatic Specific Antigen Increased				
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)		
occurrences (all)	0	1		
Red Blood Cell Sedimentation Rate Decreased				
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)		
occurrences (all)	0	1		
Transaminases Increased				
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)		
occurrences (all)	0	1		
Urine Colour Abnormal				
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)		
occurrences (all)	0	1		
Urine Output Decreased				
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)		
occurrences (all)	0	1		

Weight Decreased			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Weight Increased			
subjects affected / exposed	2 / 137 (1.46%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			
Arthropod Bite			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Arthropod Sting			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	2	
Face Injury			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Foot Fracture			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Joint Injury			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Ligament Injury			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Ligament Rupture			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Muscle Strain			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Ligament Sprain			

subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Nerve Injury			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Post Lumbar Puncture Syndrome			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Radius Fracture			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Procedural Pain			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Skin Injury			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Spinal Fracture			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Traumatic Haematoma			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Wrist Fracture			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Bundle Branch Block Right			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Cardiovascular Insufficiency			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	

Palpitations			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	5	
Sinus Bradycardia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Anosmia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Carpal Tunnel Syndrome			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Cervicobrachial Syndrome			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Cognitive Disorder			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Disturbance In Attention			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	2 / 137 (1.46%)	3 / 136 (2.21%)	
occurrences (all)	2	3	
Headache			
subjects affected / exposed	8 / 137 (5.84%)	9 / 136 (6.62%)	
occurrences (all)	9	11	
Hypoaesthesia			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Lethargy			
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)	
occurrences (all)	0	4	
Memory Impairment			

subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Migraine			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	2	
Myelopathy			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Neuropathy Peripheral			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	1 / 137 (0.73%)	3 / 136 (2.21%)	
occurrences (all)	1	3	
Parkinson's Disease			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Polyneuropathy			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Trigeminal Neuralgia			
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	

Anaemia			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	2	
Iron Deficiency Anaemia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Lymphadenopathy			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	2	
Neutropenia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Cerumen Impaction			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Vertigo			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	3 / 137 (2.19%)	2 / 136 (1.47%)	
occurrences (all)	3	3	
Dry Eye			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	2	1	
Optic Neuropathy			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Photophobia			

subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Visual Acuity Reduced			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	2	
Visual Impairment			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Abdominal Distension			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Abdominal Pain			
subjects affected / exposed	5 / 137 (3.65%)	0 / 136 (0.00%)	
occurrences (all)	5	0	
Abdominal Pain Upper			
subjects affected / exposed	2 / 137 (1.46%)	4 / 136 (2.94%)	
occurrences (all)	2	4	
Abnormal Faeces			
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)	
occurrences (all)	0	2	
Anal Inflammation			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Anal Ulcer			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Aphthous Stomatitis			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Bowel Movement Irregularity			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	

Cheilitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	3 / 137 (2.19%)	6 / 136 (4.41%)	
occurrences (all)	3	7	
Diarrhoea			
subjects affected / exposed	18 / 137 (13.14%)	10 / 136 (7.35%)	
occurrences (all)	18	10	
Dry Mouth			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	1 / 137 (0.73%)	4 / 136 (2.94%)	
occurrences (all)	2	5	
Faeces Hard			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	2	
Gastritis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	2	
Gastritis Erosive			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Gingivitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Glossodynia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	

Haematochezia			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	2	
Haemorrhoidal Haemorrhage			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Haemorrhoids			
subjects affected / exposed	4 / 137 (2.92%)	6 / 136 (4.41%)	
occurrences (all)	4	7	
Inguinal Hernia			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Mouth Ulceration			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	2	
Oral Discomfort			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Oral Disorder			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Pancreatitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Parotid Gland Enlargement			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Proctitis			
subjects affected / exposed	0 / 137 (0.00%)	4 / 136 (2.94%)	
occurrences (all)	0	5	
Rectal Discharge			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	

Rectal Polyp			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Rectal Ulcer			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Reflux Gastritis			
subjects affected / exposed	2 / 137 (1.46%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Salivary Gland Calculus			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Tooth Discolouration			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Tooth Loss			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)	
occurrences (all)	0	2	
Varices Oesophageal			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 137 (0.73%)	3 / 136 (2.21%)	
occurrences (all)	1	3	
Hepatobiliary disorders			
Hepatic Steatosis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Hepatitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Hyperbilirubinaemia			

subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acanthosis			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Acne			
subjects affected / exposed	3 / 137 (2.19%)	0 / 136 (0.00%)	
occurrences (all)	4	0	
Actinic Keratosis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Blister			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Alopecia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Dermal Cyst			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Dermatitis			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	2	
Dry Skin			
subjects affected / exposed	2 / 137 (1.46%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Eczema			
subjects affected / exposed	3 / 137 (2.19%)	4 / 136 (2.94%)	
occurrences (all)	3	4	
Erythema			
subjects affected / exposed	2 / 137 (1.46%)	1 / 136 (0.74%)	
occurrences (all)	2	1	
Hyperhidrosis			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	

Night Sweats			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	3	
Pruritus			
subjects affected / exposed	1 / 137 (0.73%)	3 / 136 (2.21%)	
occurrences (all)	1	3	
Psoriasis			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Rash			
subjects affected / exposed	7 / 137 (5.11%)	3 / 136 (2.21%)	
occurrences (all)	7	4	
Seborrhoea			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Skin Lesion			
subjects affected / exposed	4 / 137 (2.92%)	3 / 136 (2.21%)	
occurrences (all)	4	3	
Skin Burning Sensation			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)	
occurrences (all)	0	2	
Haematuria			
subjects affected / exposed	2 / 137 (1.46%)	2 / 136 (1.47%)	
occurrences (all)	2	2	
Micturition Urgency			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Nephrolithiasis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Proteinuria			

subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Renal Failure			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Renal Impairment			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Urethral Haemorrhage			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Adrenal Cyst			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Hyperparathyroidism Secondary			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Hyperprolactinaemia			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	3 / 137 (2.19%)	0 / 136 (0.00%)	
occurrences (all)	3	0	
Arthralgia			
subjects affected / exposed	7 / 137 (5.11%)	7 / 136 (5.15%)	
occurrences (all)	8	7	
Back Pain			
subjects affected / exposed	10 / 137 (7.30%)	4 / 136 (2.94%)	
occurrences (all)	10	7	
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Muscle Contracture			

subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Muscle Spasms			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Musculoskeletal Stiffness			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Musculoskeletal Pain			
subjects affected / exposed	2 / 137 (1.46%)	2 / 136 (1.47%)	
occurrences (all)	2	3	
Myalgia			
subjects affected / exposed	4 / 137 (2.92%)	1 / 136 (0.74%)	
occurrences (all)	4	1	
Neck Pain			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Osteoarthritis			
subjects affected / exposed	3 / 137 (2.19%)	0 / 136 (0.00%)	
occurrences (all)	3	0	
Osteoporosis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Pain In Extremity			
subjects affected / exposed	4 / 137 (2.92%)	0 / 136 (0.00%)	
occurrences (all)	4	0	
Pain In Jaw			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Shoulder Deformity			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Spinal Osteoarthritis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Tendon Disorder			

subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Tendonitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Infections and infestations			
Abscess Sweat Gland			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Acarodermatitis			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Acute Sinusitis			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Anal Abscess			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Anal Chlamydia Infection			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Bacterial Infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	4 / 137 (2.92%)	3 / 136 (2.21%)	
occurrences (all)	4	3	
Candidiasis			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Cellulitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Chlamydial Infection			
subjects affected / exposed	3 / 137 (2.19%)	1 / 136 (0.74%)	
occurrences (all)	5	1	

Conjunctivitis Bacterial			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Ear Infection			
subjects affected / exposed	2 / 137 (1.46%)	1 / 136 (0.74%)	
occurrences (all)	2	1	
Cystitis			
subjects affected / exposed	2 / 137 (1.46%)	0 / 136 (0.00%)	
occurrences (all)	5	0	
Eye Infection			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Febrile Infection			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Folliculitis			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Fungal Infection			
subjects affected / exposed	2 / 137 (1.46%)	2 / 136 (1.47%)	
occurrences (all)	2	2	
Fungal Skin Infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	2 / 137 (1.46%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Gastric Infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis Shigella			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Gastroenteritis Norovirus			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	

Gingival Abscess			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Genital Herpes			
subjects affected / exposed	1 / 137 (0.73%)	3 / 136 (2.21%)	
occurrences (all)	1	4	
Gastroenteritis Viral			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Gonorrhoea			
subjects affected / exposed	3 / 137 (2.19%)	2 / 136 (1.47%)	
occurrences (all)	3	2	
Helicobacter Gastritis			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Hepatitis C			
subjects affected / exposed	2 / 137 (1.46%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Herpes Simplex			
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)	
occurrences (all)	0	2	
Herpes Zoster			
subjects affected / exposed	6 / 137 (4.38%)	1 / 136 (0.74%)	
occurrences (all)	6	1	
Hordeolum			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Impetigo			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Infection Parasitic			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	

Influenza			
subjects affected / exposed	4 / 137 (2.92%)	6 / 136 (4.41%)	
occurrences (all)	4	7	
Latent Syphilis			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Laryngitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Localised Infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	4	0	
Latent Tuberculosis			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 137 (0.73%)	3 / 136 (2.21%)	
occurrences (all)	1	3	
Lower Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Molluscum Contagiosum			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	16 / 137 (11.68%)	11 / 136 (8.09%)	
occurrences (all)	21	12	
Onychomycosis			
subjects affected / exposed	4 / 137 (2.92%)	3 / 136 (2.21%)	
occurrences (all)	4	3	
Oral Herpes			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Oropharyngeal Gonococcal Infection			

subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Otitis Externa			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Otitis Media			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Papilloma Viral Infection			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Pharyngitis			
subjects affected / exposed	3 / 137 (2.19%)	3 / 136 (2.21%)	
occurrences (all)	3	3	
Pneumonia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Proctitis Bacterial			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Proctitis Chlamydial			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Proctitis Gonococcal			
subjects affected / exposed	2 / 137 (1.46%)	1 / 136 (0.74%)	
occurrences (all)	2	2	
Pyelonephritis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Rash Pustular			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Respiratory Tract Infection			
subjects affected / exposed	3 / 137 (2.19%)	3 / 136 (2.21%)	
occurrences (all)	4	3	
Rhinitis			

subjects affected / exposed	6 / 137 (4.38%)	5 / 136 (3.68%)	
occurrences (all)	6	5	
Shigella Infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	3 / 137 (2.19%)	5 / 136 (3.68%)	
occurrences (all)	3	5	
Skin Infection			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Syphilis			
subjects affected / exposed	4 / 137 (2.92%)	5 / 136 (3.68%)	
occurrences (all)	8	5	
Tinea Pedis			
subjects affected / exposed	0 / 137 (0.00%)	2 / 136 (1.47%)	
occurrences (all)	0	2	
Tinea Versicolour			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	1 / 137 (0.73%)	3 / 136 (2.21%)	
occurrences (all)	1	4	
Tonsillitis Bacterial			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Tooth Abscess			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Tooth Infection			
subjects affected / exposed	2 / 137 (1.46%)	1 / 136 (0.74%)	
occurrences (all)	2	1	
Tracheitis			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Trichomoniasis			

subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 137 (0.73%)	5 / 136 (3.68%)	
occurrences (all)	2	5	
Upper Respiratory Tract Infection Bacterial			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Urethritis			
subjects affected / exposed	4 / 137 (2.92%)	0 / 136 (0.00%)	
occurrences (all)	6	0	
Urethritis Chlamydial			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Urethritis Gonococcal			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Urinary Tract Infection			
subjects affected / exposed	4 / 137 (2.92%)	2 / 136 (1.47%)	
occurrences (all)	4	2	
Viral Infection			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Viral Pharyngitis			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Dyslipidaemia			

subjects affected / exposed	2 / 137 (1.46%)	0 / 136 (0.00%)	
occurrences (all)	2	0	
Gout			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Hypercholesterolaemia			
subjects affected / exposed	7 / 137 (5.11%)	0 / 136 (0.00%)	
occurrences (all)	7	0	
Hypercreatininaemia			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Hyperlipasaemia			
subjects affected / exposed	1 / 137 (0.73%)	0 / 136 (0.00%)	
occurrences (all)	1	0	
Hyperlipidaemia			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	3	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	2	
Hypocalcaemia			
subjects affected / exposed	0 / 137 (0.00%)	1 / 136 (0.74%)	
occurrences (all)	0	1	
Hypophosphataemia			
subjects affected / exposed	1 / 137 (0.73%)	2 / 136 (1.47%)	
occurrences (all)	1	2	
Obesity			
subjects affected / exposed	1 / 137 (0.73%)	1 / 136 (0.74%)	
occurrences (all)	1	1	
Hypovitaminosis			
subjects affected / exposed	2 / 137 (1.46%)	3 / 136 (2.21%)	
occurrences (all)	2	3	
Vitamin D Deficiency			
subjects affected / exposed	2 / 137 (1.46%)	1 / 136 (0.74%)	
occurrences (all)	2	1	
Weight Fluctuation			

subjects affected / exposed occurrences (all)	1 / 137 (0.73%) 1	0 / 136 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2011	Amendment I: The overall reason for the amendment was to change inclusion criterion 4 so that participants willing to participate could also have switched between classes in their previous highly active antiretroviral therapy (HAART) regimen and not only within class.
24 May 2012	Amendment II: The overall reason for the amendment was to prohibit the concomitant use of telaprevir or boceprevir for participating participants co-infected with hepatitis C, based on new drug-drug interaction data.
26 October 2012	Amendment III: The overall reason for the amendment was to clarify inclusion criterion 8, so that participants could not have CD4+ cell counts below 100 cells/millimeter3 (mm3) from the time of first known HIV infection to the start of HAART, and had to have more than 200 cells/mm3 at screening or a maximum of 4 weeks prior to screening.
09 July 2014	Amendment IV: The primary efficacy analysis at Week 48 indicated that switching to DRV/rtv monotherapy showed lower efficacy versus triple antiretroviral therapy (86% versus 95%). However, lower efficacy was seen only in participants with CD4+ nadir levels less than (<)200 cells/microliters (mcL). Having reviewed these data, the independent Data and Safety Monitoring Board (DSMB) advised that, participants in the monotherapy arm who entered the study with a nadir CD4+ count <200 cells/mcL should also receive 2 nucleoside analogues (N[t]RTIs).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported