Clinical trial results:
A Phase IIIb, randomized, open-label study of the safety and efficacy of GSK1349572 (dolutegravir, DTG) 50 mg once daily compared to darunavir/ritonavir (DRV/r) 800 mg/100 mg once daily each administered with fixed-dose dual nucleoside reverse transcriptase inhibitor therapy over 96 weeks in HIV-1 infected antiretroviral naïve adult subjects.

Summary

EudraCT number	2011-003629-86
Trial protocol	ES IT
Global end of trial date	26 December 2016

Results information

Result version number	v1 (current)
This version publication date	30 December 2017
First version publication date	30 December 2017

Trial information

Trial identification

Sponsor protocol code	114915

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ViiV Healthcare
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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	05 July 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 April 2013
Global end of trial reached?	Yes
Global end of trial date	26 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferior antiviral activity of DTG 50 milligram (mg) administered once daily compared to DRV/r 800 mg/100 mg once daily over 48 weeks in Human Immunodeficiency Virus Type-1 (HIV-1) infected therapy-naïve participants.

Protection of trial subjects:

99999

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	54 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 213
Country: Number of subjects enrolled	Spain: 86
Country: Number of subjects enrolled	France: 52
Country: Number of subjects enrolled	Italy: 49
Country: Number of subjects enrolled	Romania: 21
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Russian Federation: 18
Country: Number of subjects enrolled	Switzerland: 13
Country: Number of subjects enrolled	Puerto Rico: 12
Worldwide total number of subjects	484
EEA total number of subjects	228

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)	480
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a 2 sequential treatment period study. In first period (Randomization phase) participants received either dolutegravir (DTG) 50 milligram (mg) or darunavir (DRV) 800 mg with ritonavir (RTV) 100 mg once daily (QD) for 96 weeks. DTG participants who completed 96 Weeks of DTG then continued to receive DTG 50 mg in Extension phase.

Pre-assignment

Screening details:

A total of 595 participants were screened; 107 were screen failures; 488 were randomized; 485 received at least 1 dose of study medication and comprised the Intent-To-Treat exposed (ITT-E) population of which 1 participant was removed, creating the modified ITT-E population with 484 participants. 123 participants enrolled in Extension Phase.

Period 1

Period 1 title	Randomization Phase 96 week
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	DTG 50 mg QD

Arm description:

Participants received DTG 50 mg QD administered in combination with FDC dual NRTI therapy (either ABC/3TC or TDF/FTC) for 96 weeks. Participants were then given the opportunity to receive DTG 50 mg QD during an Extension Phase of the study.

Arm type	Experimental
Investigational medicinal product name	Dolutegravir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received once daily dolutegravir 50 mg oral tablets

Investigational medicinal product name	Tenofovir/Emtricitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received fixed dose combination of tenofovir/emtricitabine oral tablets

Investigational medicinal product name	Abacavir/Lamivudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received fixed dose combination of abacavir/lamivudine oral tablets

Arm title	DRV 800 mg + RTV 100 mg QD

Arm description:

Participants received DRV 800 mg + RTV 100 mg QD administered in combination with FDC dual NRTI

therapy (either ABC/3TC or TDF/FTC) for 96 weeks.

Arm type	Active comparator
Investigational medicinal product name	Ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use
Dosage and administration details: Participants received once daily ritonavir 100 mg oral tablets	
Investigational medicinal product name	Darunavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use
Dosage and administration details: Participants received 2 oral tablets of 400 mg darunavir once daily	
Investigational medicinal product name	Abacavir/Lamivudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use
Dosage and administration details: Participants received fixed dose combination of abacavir/lamivudine oral tablets	
Investigational medicinal product name	Tenofovir/Emtricitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use
Dosage and administration details: Participants received fixed dose combination of tenofovir/emtricitabine oral tablets	

Number of subjects in period 1	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD
Started	242	242
Completed	209	189
Not completed	33	53
Adverse event, serious fatal	1	-
Consent withdrawn by subject	2	8
Physician decision	2	3
Adverse event, non-fatal	4	13
Other: study closed/terminated	-	1
Protocol-defined Stopping Criteria	1	-
Lost to follow-up	15	18
Lack of efficacy	3	4
Protocol deviation	5	6

Period 2

Period 2 title	Extension Phase approximately 3 years
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Extension DTG 50 mg

Arm description:

DTG participants who successfully completed 96 Weeks of randomized phase continued to receive DTG 50 mg QD during Extension phase

Arm type	Experimental
Investigational medicinal product name	Dolutegravir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received once daily dolutegravir 50 mg oral tablets

Investigational medicinal product name	Abacavir/Lamivudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received fixed dose combination of abacavir/lamivudine oral tablets

Investigational medicinal product name	Tenofovir/Emtricitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received fixed dose combination of tenofovir/emtricitabine oral tablets

Number of subjects in period 2	Extension DTG 50 mg
Started	123
Completed	115
Not completed	8
Adverse event, non-fatal	2
Lost to follow-up	4
Lack of efficacy	2

Baseline characteristics

Reporting groups	
Reporting group title	DTG 50 mg QD
Reporting group description:	
Participants received DTG 50 mg QD administered in combination with FDC dual NRTI therapy (either ABC/3TC or TDF/FTC) for 96 weeks. Participants were then given the opportunity to receive DTG 50 mg QD during an Extension Phase of the study.	
Reporting group title	DRV 800 mg + RTV 100 mg QD
Reporting group description:	
Participants received DRV 800 mg + RTV 100 mg QD administered in combination with FDC dual NRTI therapy (either ABC/3TC or TDF/FTC) for 96 weeks.	

Reporting group values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD	Total
Number of subjects	242	242	484
Age categorical			
Units: Subjects			
Age continuous			
Results from the mITT-E Population are presented in this report.			
Units: years			
arithmetic mean	35.7	36.2	
standard deviation	± 10.66	± 10.64	-
Gender categorical			
Results from the mITT-E are presented in this report.			
Units: Subjects			
Female	31	41	72
Male	211	201	412
Race/Ethnicity, Customized			
Results from the mITT-E are presented in this report.			
Units: Subjects			
African American/African Heritage	60	53	113
American Indian or Alaska Native	3	9	12
Asian - Central/South Asian Heritage	0	1	1
Asian - Japanese Heritage	1	0	1
Asian - South East Asian Heritage	1	0	1
Native Hawaiian or other Pacific Islander	2	0	2
White - Arabic/North African Heritage	4	3	7
White - White/Caucasian/European Heritage	169	173	342
Mixed Race	1	3	4
Missing	1	0	1

End points

End points reporting groups

Reporting group title	DTG 50 mg QD
Reporting group description:	
Participants received DTG 50 mg QD administered in combination with FDC dual NRTI therapy (either ABC/3TC or TDF/FTC) for 96 weeks. Participants were then given the opportunity to receive DTG 50 mg QD during an Extension Phase of the study.	
Reporting group title	DRV 800 mg + RTV 100 mg QD
Reporting group description:	
Participants received DRV 800 mg + RTV 100 mg QD administered in combination with FDC dual NRTI therapy (either ABC/3TC or TDF/FTC) for 96 weeks.	
Reporting group title	Extension DTG 50 mg
Reporting group description:	
DTG participants who successfully completed 96 Weeks of randomized phase continued to receive DTG 50 mg QD during Extension phase	

Primary: Percentage of participants with Plasma Human Immunodeficiency Virus-1 (HIV-1) Ribonucleic Acid (RNA) <50 copies/milliliter (c/mL) at Week 48

End point title	Percentage of participants with Plasma Human Immunodeficiency Virus-1 (HIV-1) Ribonucleic Acid (RNA) <50 copies/milliliter (c/mL) at Week 48
End point description:	
Assessment was done using Missing, Switch or Discontinuation = Failure (MSDF), as codified by the Food and Drug Administration (FDA) "snapshot" algorithm.This algorithm treated all participants without HIV-1 RNA data at Week 48 as nonresponders, as well as participants who switched their concomitant ART prior to Week 48 as follows: background ART substitutions non-permitted per protocol (one background ART substitution was permitted for safety or tolerability); background ART substitutions permitted per protocol unless the decision to switch was documented as being before or at the first on-treatment visit where HIV-1 RNA was assessed. Otherwise, virologic success or failure was determined by the last available HIV-1 RNA assessment while the participant was on-treatment in the snapshot window (Week 48 +/- 6 weeks). Modified Intent-To-Treat Exposed (mITT-E) Population:all randomized participants who received at least one dose of investigational product	
End point type	Primary
End point timeframe:	
Week 48	

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	242		
Units: Percentage of participants				
Percentage of participants	90	83		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	DRV 800 mg + RTV 100 mg QD v DTG 50 mg QD
Number of subjects included in analysis	484
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.025 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	7.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	13.2

Notes:

[1] - Non-inferiority of DTG 50 mg and DRV+RTV at Week 48 can be concluded if the lower bound of a two-sided 95% confidence interval (CI) for the difference in percentages (DTG - DRV+RTV) is greater than -12%. If non-inferiority is established, superiority can be tested at the nominal 5% level based on a pre-specified testing procedure.
[2] - P-value is for test of superiority.

Secondary: Time to virologic suppression (<50 copies/mL) through Week 48

End point title	Time to virologic suppression (<50 copies/mL) through Week 48

End point description:

The time to viral suppression (i.e. first viral load value <50 copies/mL) through Week 48 was derived and summarized using Kaplan-Meier plots. Participants who withdrew for any reason without having suppressed prior to the analysis were censored. Confidence intervals were estimated using the Brookmeyer-Crowley method. 99999 indicates the value was not available for the indicated time point

End point type	Secondary

End point timeframe:

From Baseline through Week 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	242		
Units: Days				
median (confidence interval 95%)				
Days	28.0 (-99999 to 99999)	85.0 (84.0 to 108.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with plasma HIV-1 RNA <400 c/mL at Week 48

End point title	Percentage of participants with plasma HIV-1 RNA <400 c/mL at Week 48

End point description:

The percentage of participants with Plasma HIV-1 RNA <400 c/mL at Week 48 was assessed MSDF, as codified by the FDA "snapshot" algorithm. This algorithm treated all participants without HIV-1 RNA data at Week 48 as nonresponders, as well as participants who switched their concomitant ART prior to Week 48 as follows: background ART substitutions non-permitted per protocol (one background ART substitution was permitted for safety or tolerability); background ART substitutions permitted per protocol unless the decision to switch was documented as being before or at the first on-treatment visit where HIV-1 RNA was assessed. Otherwise, virologic success or failure was determined by the last available HIV-1 RNA assessment while the participant was on-treatment in the snapshot window (Week 48 +/- 6 weeks).

End point type	Secondary

End point timeframe:

Week 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	242		
Units: Percentage of participants				
Percentage of participants	92	87		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in plasma HIV-1 RNA (log10 c/mL) at Weeks 4, 8, 12, 16, 24, 36 and 48

End point title	Change from Baseline in plasma HIV-1 RNA (log10 c/mL) at Weeks 4, 8, 12, 16, 24, 36 and 48

End point description:

Change from Baseline in plasma HIV-1 RNA (log10 c/mL) was assessed at Weeks 4, 8, 12, 16, 24, 36 and 48 . Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles). Different participants may have been analyzed for different visits, so the overall number of participants analyzed reflects everyone in the mITT-E Population.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 24, 36 and 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242[3]	242[4]		
Units: Log10 copies per mL				
arithmetic mean (standard deviation)				
Week 4, n=238, 235	-2.80 (± 0.625)	-2.01 (± 0.454)		
Week 8, n=237, 236	-2.86 (± 0.649)	-2.40 (± 0.524)		
Week 12, n=234, 227	-2.88 (± 0.653)	-2.61 (± 0.537)		
Week 16, n=229, 228	-2.86 (± 0.691)	-2.71 (± 0.618)		
Week 24, n=234, 227	-2.86 (± 0.765)	-2.83 (± 0.663)		
Week 36, n=232, 218	-2.87 (± 0.715)	-2.85 (± 0.683)		
Week 48, n=227, 212	-2.89 (± 0.739)	-2.86 (± 0.663)		

Notes:

[3] - mITT-E Population.

[4] - mITT-E Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4+ and CD8+ cell counts

End point title	Change from Baseline in CD4+ and CD8+ cell counts

End point description:

Change from Baseline in CD4+ cell counts was assessed at Weeks 4, 8, 12, 16, 36 and 48. Change from Baseline in CD8+ cell counts was assessed at Weeks 4, 12, 24 and 48. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles). Different participants may have been analyzed for different visits and parameters, so the overall number of participants analyzed reflects everyone in the mITT-E Population.

End point type	Secondary

End point timeframe:

Baseline and Weeks 4, 8, 12, 16, 36 and 48 for CD4+ and Baseline and Weeks 4, 12, 24 and 48 for CD8+

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	242		
Units: Cells per millimeters cubed (cells/mm^3)				
arithmetic mean (standard deviation)				
CD4+ cell count, Week 4, n=237, 236	80.1 (± 101.36)	75.6 (± 124.36)		
CD4+ cell count, Week 8, n=236, 236	126.9 (± 124.13)	118.8 (± 142.54)		

CD4+ cell count, Week 12, n=234, 228	135.2 (± 120.03)	131.8 (± 143.88)		
CD4+ cell count, Week 16, n=227, 227	156.8 (± 146.60)	146.1 (± 166.08)		
CD4+ cell count, Week 24, n=233, 227	165.1 (± 145.85)	164.3 (± 180.00)		
CD4+ cell count, Week 36, n=232, 218	206.1 (± 159.06)	186.5 (± 183.61)		
CD4+ cell count, Week 48, n=227, 212	243.8 (± 180.68)	215.4 (± 177.26)		
CD8+ cell count, Week 4, n=235, 235	-47.4 (± 276.01)	-3.7 (± 375.94)		
CD8+ cell count, Week 12, n=231, 227	-42.0 (± 343.81)	-68.9 (± 373.38)		
CD8+ cell count, Week 24, n=231, 224	-108.0 (± 350.03)	-132.9 (± 389.70)		
CD8+ cell count, Week 48, n=224, 210	-109.5 (± 360.94)	-162.1 (± 421.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with HIV-1 associated disease progression with the indicated shift to CDC Class C, or New CDC Class C or Death at Week 48

End point title	Number of Participants with HIV-1 associated disease progression with the indicated shift to CDC Class C, or New CDC Class C or Death at Week 48

End point description:

The number of participants with HIV-1 disease progression (AIDS or death) was assessed per the Centers for Disease Control and Prevention (CDC) 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. The CDC classifies HIV infection as Category A (participants with asymptomatic HIV infection, acute HIV infection with accompanying illness, or persistent generalized lymphadenopathy), Category B (participants with symptomatic non-AIDS condition, i.e., conditions that are attributed to HIV infection or are indicative of a defect in cell-mediated immunity; or conditions are considered by physicians to have a clinical course or to require management that is complicated by HIV infection), and Category C (includes AIDS indicator conditions as defined by diagnostic or presumptive measures).

End point type	Secondary

End point timeframe:

Week 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	242		
Units: Participants				
Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in fasting low-density lipoprotein (LDL) cholesterol through Week 48

End point title	Change From Baseline in fasting low-density lipoprotein (LDL) cholesterol through Week 48

End point description:

Fasting LDL cholesterol change from Baseline was analyzed. Values represented are for adjusted means. Estimates are calculated from a repeated measures model including the following covariates: treatment, visit, Baseline plasma HIV-1 RNA, background dual NRTI therapy, Baseline LDL cholesterol, treatment*visit interaction and Baseline LDL cholesterol*visit interaction. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

From Baseline through Week 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	178		
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard error)				
Millimoles per liter (mmol/L)	0.07 (± 0.041)	0.37 (± 0.041)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Grade 2 or higher abnormalities in fasting LDL cholesterol through Week 48

End point title	Percentage of participants with Grade 2 or higher abnormalities in fasting LDL cholesterol through Week 48

End point description:

Hematology and clinical chemistry data were summarized according to the division of AIDS (DAIDS) table for grading the Severity of adverse events, version 1.0. Grade 1, Mild; Grade 2, Moderate; Grade 3 (G3), Severe; Grade 4 (G4), Life-threatening or disabling; Grade 5, Death. Data are presented for which an increase in fasting LDL cholesterol to Grade 2 or higher occurred. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

From Baseline through Week 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	242		
Units: Percentage of Participants				
Percentage of Participants	2	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated Grade 3 and Grade 4 maximum post-Baseline chemistry and hematology laboratory toxicities

End point title	Number of participants with the indicated Grade 3 and Grade 4 maximum post-Baseline chemistry and hematology laboratory toxicities

End point description:

Hematology and clinical chemistry data were summarized according to the division of AIDS (DAIDS) table for grading the Severity of adverse events, version 1.0. Grade 1, Mild; Grade 2, Moderate; Grade 3 (G3), Severe; Grade 4 (G4), Life-threatening or disabling; Grade 5, Death. Data are presented for only those parameters for which an increase to Grade 3 or Grade 4 occurred.

End point type	Secondary

End point timeframe:

From Baseline through Week 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	242		
Units: Participants				
Alanine Amino Transferase, G3	2	1		
Alanine Amino Transferase, G4	1	3		
Aspartate Amino Transferase, G3	6	3		
Aspartate Amino Transferase, G4	2	0		
Cholesterol, G3	0	3		
Creatine Kinase, G3	8	5		
Creatine Kinase, G4	8	4		
Hyperglycaemia, G3	1	2		
Hypoglycaemia, G3	0	1		
LDL Cholesterol, G3	2	6		
Lipase, G3	5	5		
Lipase, G4	2	0		
Phosphorus, inorganic, G3	7	7		
Total Bilirubin, G3	1	0		
Triglycerides, G3	1	2		
Triglycerides, G4	0	1		
Hemoglobin, G3	1	0		

Hemoglobin, G4	1	0		
Platelet count, G4	0	1		
Total Neutrophils, G3	5	0		
Total Neutrophils, G4	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants (par.) with detectable virus that has genotypic or phenotypic evidence of treatment-emergent resistance to DTG, DRV+RTV and other on-study ART at time of protocol defined virology failure (PDVF)

End point title	Number of participants (par.) with detectable virus that has genotypic or phenotypic evidence of treatment-emergent resistance to DTG, DRV+RTV and other on-study ART at time of protocol defined virology failure (PDVF)

End point description:

An assessment was made of every change across all amino acids within the integrase (IN), reverse transcriptase (RT), and Protease (PRO) encoding region at Baseline and at time of suspected PDVF. PDVF is defined as the confirmed plasma HIV-1 RNA >200 c/mL >=Week 24. PDVF Genotypic Population included all participants in the mITT-E population with available on-treatment genotypic resistance data, at time of PDVF. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Baseline until PDVF up to Week 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2[5]	2[6]		
Units: Participants				
Participants	0	0		

Notes:

[5] - PDVF Genotypic Population

[6] - PDVF Genotypic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Acquired Immune Deficiency Syndrome (AIDS) Clinical Trials Group (ACTG) Symptom Distress Module (SDM) bother score at Week 4, Week 24, and Week 48

End point title	Change from Baseline in Acquired Immune Deficiency Syndrome (AIDS) Clinical Trials Group (ACTG) Symptom Distress Module (SDM) bother score at Week 4, Week 24, and Week 48

End point description:

SDM is a 20-item self-reported measure that addresses the presence and perceived distress linked to symptoms commonly associated with HIV or its treatment. Each item is rated from 0 to 4 where 0

(complete absence of symptom) and 4 (very bothersome symptom). Overall score calculated as the sum of the scores for each of the 20 items of the questionnaire and ranged from 0 (best health) and 80 (worst health). Values represented are for adjusted mean. Estimates are calculated from an ANCOVA model adjusting for age, sex, race, baseline viral load, background dual NRTI therapy and baseline symptom bother score. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. A positive change from Baseline indicates a decline in a participant's quality of life over that period.

End point type	Secondary

End point timeframe:

Baseline, Week 4, Week 24, and Week 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	242		
Units: Scores on a scale				
arithmetic mean (standard error)				
Week 4, n=218, 210	-3.20 (± 0.56)	-2.19 (± 0.56)		
Week 24, n=222, 214	-2.71 (± 0.64)	-1.65 (± 0.65)		
Week 48, n= 222, 215	-2.46 (± 0.68)	-0.77 (± 0.69)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in European Quality of Life -5 Dimensions (EQ-5D) utility scores at Week 24 and Week 48

End point title	Change from Baseline in European Quality of Life -5 Dimensions (EQ-5D) utility scores at Week 24 and Week 48

End point description:

The EQ-5D is a 5-question quality of life instrument that provides a utility score and visual analogue scale score that describes the participants' health status. The primary reason for including the EQ-5D is to elicit utility values for potential cost-effectiveness analysis for submission to health technology assessment agencies. The EQ-5D total score ranges from 0 (worst health state) to 1 (perfect health state) and 1 reflects the best outcome. Values represented are for adjusted mean. Estimates are calculated from an ANCOVA model adjusting for age, sex, race, baseline viral load, background dual NRTI therapy and Baseline EQ-5D utility score. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline, Week 24, and Week 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	242		
Units: Scores on a scale				
arithmetic mean (standard error)				
Week 24, n=217, 213	0.00 (± 0.012)	0.02 (± 0.012)		
Week 48, n=224, 217	0.01 (± 0.012)	0.01 (± 0.012)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in EQ-5D thermometer scores at Week 24 and Week 48

End point title	Change from Baseline in EQ-5D thermometer scores at Week 24 and Week 48

End point description:

The European Quality of Life -5 Dimensions (EQ-5D) is a 5-question quality of life instrument that provides a utility score and visual analogue scale score that describes the participants' health status. The primary reason for including the EQ-5D is to elicit utility values for potential cost-effectiveness analysis for submission to health technology assessment agencies. Thermometer score is based on a visual analogue scale (VAS) ranging from 100 (best imaginable health state) to 0 (worst imaginable health state).Values represented are for adjusted mean. Estimates are calculated from an ANCOVA model adjusting for age, sex, race, Baseline viral load, background dual NRTI therapy and Baseline EQ-5D thermometer score. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline, Week 24, and Week 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	242		
Units: Scores on a scale				
arithmetic mean (standard error)				
Week 24, n=221, 216	4.95 (± 0.885)	5.96 (± 0.895)		
Week 48, n=224, 220	5.78 (± 0.762)	6.95 (± 0.769)		

Statistical analyses

No statistical analyses for this end point

Secondary: Human Immunodeficiency Virus Treatment Satisfaction Questionnaire

(HIVTSQ) total score at Week 4, Week 24, and Week 48

End point title	Human Immunodeficiency Virus Treatment Satisfaction Questionnaire (HIVTSQ) total score at Week 4, Week 24, and Week 48

End point description:

Participant treatment satisfaction was measured using the self-reported scale (HIVTSQ), which consists of 10 items (1-satisfaction, 2-HIV control, 3-adverse effects, 4-level of demand, 5-convenience, 6-flexibility, 7-knowledge, 8-life habits, 9-recommendability, and 10-willingness to continue). Items are scored from 0 (very dissatisfied) to 6 (very satisfied), other than item 4, which has an inverted score from 6 (very demanding) to 0 (very undemanding). The treatment satisfaction score (range: 0-60) was the sum of the individual items. HIVTSQ mITT-E Population=Only participants from USA, France, Germany, Italy, Spain for whom valid translations were available from the mITT-E Population. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles). Different participants may have been analyzed for different visits, so the overall number of participants analyzed reflects everyone in the HIVTSQ mITT-E population.

End point type	Secondary

End point timeframe:

Week 4, Week 24, and Week 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	206		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 4, n=206, 192	54.1 (± 6.43)	52.4 (± 7.94)		
Week 24, n= 211, 200	56.1 (± 5.16)	54.3 (± 6.94)		
Week 48, n=212, 201	56.1 (± 4.60)	54.5 (± 6.78)		

Statistical analyses

No statistical analyses for this end point

Secondary: Human Immunodeficiency Virus Treatment Satisfaction Questionnaire (HIVTSQ) lifestyle/ease sub score at Week 4, Week 24, and Week 48

End point title	Human Immunodeficiency Virus Treatment Satisfaction Questionnaire (HIVTSQ) lifestyle/ease sub score at Week 4, Week 24, and Week 48

End point description:

Participant treatment satisfaction was measured using the self-reported scale (HIVTSQ), which consists of 10 items (1-satisfaction, 2-HIV control, 3-adverse effects, 4-level of demand, 5-convenience, 6-flexibility, 7-knowledge, 8-life habits, 9-recommendability, and 10-willingness to continue). Items are scored from 0 (very dissatisfied) to 6 (very satisfied), other than item 4, which has an inverted score from 6 (very demanding) to 0 (very undemanding). The lifestyle/ease score is the sum of items 4, 5, 6, 7 and 8 (range: 0-30). Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles). Different participants may have been analyzed for different visits, so the overall number of participants analyzed reflects everyone in the HIVTSQ mITT-E population.

End point type	Secondary

End point timeframe:

Week 4, Week 24, and Week 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	206		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 4, n=202, 190	26.7 (± 3.61)	25.8 (± 4.48)		
Week 24, n=210, 199	27.5 (± 3.16)	26.6 (± 4.11)		
Week 48, n=211, 201	27.6 (± 3.00)	26.6 (± 4.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Human Immunodeficiency Virus Treatment Satisfaction Questionnaire (HIVTSQ) convenience score at Week 4, Week 24, and Week 48

End point title	Human Immunodeficiency Virus Treatment Satisfaction Questionnaire (HIVTSQ) convenience score at Week 4, Week 24, and Week 48

End point description:

Participant treatment satisfaction was measured using the self-reported scale (HIVTSQ), which consists of 10 items (1-satisfaction, 2-HIV control, 3-adverse effects, 4-level of demand, 5-convenience, 6-flexibility, 7-knowledge, 8-life habits, 9-recommendability, and 10-willingness to continue). Items are scored from 0 (very dissatisfied) to 6 (very satisfied), other than item 4, which has an inverted score from 6 (very demanding) to 0 (very undemanding). The convenience score is the score for item 5 (range: 0-6). Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles). Different participants may have been analyzed for different visits, so the overall number of participants analyzed reflects everyone in the HIVTSQ mITT-E population.

End point type	Secondary

End point timeframe:

Week 4, Week 24, and Week 48

End point values	DTG 50 mg QD	DRV 800 mg + RTV 100 mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	206		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 4, n=204, 190	5.6 (± 0.71)	5.2 (± 1.11)		
Week 24, n=211, 200,	5.6 (± 0.64)	5.4 (± 1.01)		
Week 48, n=212, 201	5.7 (± 0.62)	5.4 (± 1.02)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) are presented from the available safety data from the start of the study medication up to end of study.

Adverse event reporting additional description:

SAEs and non-serious AEs were reported for members of the Modified Safety Population, comprised of all participants who received at least one dose of investigational product excluding one participant at one site, which was closed due to GCP non-compliance issues in another ViiV Healthcare sponsored trial.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	DRV 800 mg + RTV 100 mg QD

Reporting group description:

Participants received DRV 800 mg + RTV 100 mg QD administered in combination with FDC dual NRTI therapy (either ABC/3TC or TDF/FTC) for 96 weeks.

Reporting group title	DTG 50 mg QD

Reporting group description:

Participants received DTG 50 mg QD administered in combination with FDC dual NRTI therapy (either ABC/3TC or TDF/FTC) for 96 weeks. Participants were then given the opportunity to receive DTG 50 mg QD during an Extension Phase of the study.

Reporting group title	Extension DTG 50 mg

Reporting group description:

DTG participants who successfully completed 96 Weeks of randomized phase continued to receive DTG 50 mg QD during Extension phase

Serious adverse events	DRV 800 mg + RTV 100 mg QD	DTG 50 mg QD	Extension DTG 50 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 242 (8.68%)	36 / 242 (14.88%)	4 / 123 (3.25%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complication of pregnancy			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug hypersensitivity			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 242 (0.00%)	3 / 242 (1.24%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			

subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Drug use disorder			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back injury			
subjects affected / exposed	0 / 242 (0.00%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative ileus			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stab wound			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			

subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiomyopathy alcoholic			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congestive cardiomyopathy			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			

subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar stroke			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Methaemoglobinaemia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea haemorrhagic			

subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Odynophagia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			

subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 242 (0.00%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myofascial pain syndrome			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyarthritis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acute hepatitis C			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute sinusitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster disseminated			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster infection neurological			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurosyphilis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perineal abscess			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis infectious			

subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	DRV 800 mg + RTV 100 mg QD	DTG 50 mg QD	Extension DTG 50 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	214 / 242 (88.43%)	221 / 242 (91.32%)	52 / 123 (42.28%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	13 / 242 (5.37%)	8 / 242 (3.31%)	1 / 123 (0.81%)
occurrences (all)	17	10	1
Lipoma			
subjects affected / exposed	2 / 242 (0.83%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	2	2	0
Melanocytic naevus			
subjects affected / exposed	3 / 242 (1.24%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	3	1	0
Basal cell carcinoma			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Seborrhoeic keratosis			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	3	0	0
Skin papilloma			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Acrochordon			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Fibroma			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Oral neoplasm			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Papilloma			

subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	10 / 242 (4.13%)	7 / 242 (2.89%)	0 / 123 (0.00%)
occurrences (all)	10	7	0
Hot flush			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Varicose vein			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Deep vein thrombosis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Haematoma			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Hypertensive crisis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Pregnancy, puerperium and perinatal conditions			
Vomiting in pregnancy			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	16 / 242 (6.61%)	16 / 242 (6.61%)	0 / 123 (0.00%)
occurrences (all)	17	17	0
Fatigue			
subjects affected / exposed	14 / 242 (5.79%)	15 / 242 (6.20%)	0 / 123 (0.00%)
occurrences (all)	15	17	0
Asthenia			

subjects affected / exposed	11 / 242 (4.55%)	5 / 242 (2.07%)	2 / 123 (1.63%)
occurrences (all)	11	7	2
Influenza like illness			
subjects affected / exposed	6 / 242 (2.48%)	9 / 242 (3.72%)	0 / 123 (0.00%)
occurrences (all)	7	11	0
Chest pain			
subjects affected / exposed	7 / 242 (2.89%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	8	3	0
Pain			
subjects affected / exposed	5 / 242 (2.07%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	6	3	0
Chills			
subjects affected / exposed	4 / 242 (1.65%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	4	2	0
Feeling hot			
subjects affected / exposed	4 / 242 (1.65%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	5	2	0
Malaise			
subjects affected / exposed	2 / 242 (0.83%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	2	3	0
Peripheral swelling			
subjects affected / exposed	2 / 242 (0.83%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	2	3	0
Local swelling			
subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Chest discomfort			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Discomfort			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Thirst			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Abscess sterile			

subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Axillary pain			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Cyst			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Dysplasia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Feeling abnormal			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Hunger			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Nodule			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Submandibular mass			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Thirst decreased			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Vaccination site erythema			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0

Immune system disorders			
Seasonal allergy			
subjects affected / exposed	3 / 242 (1.24%)	3 / 242 (1.24%)	1 / 123 (0.81%)
occurrences (all)	3	3	1
Hypersensitivity			
subjects affected / exposed	1 / 242 (0.41%)	4 / 242 (1.65%)	1 / 123 (0.81%)
occurrences (all)	1	5	1
Multiple allergies			
subjects affected / exposed	3 / 242 (1.24%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	3	1	0
Drug hypersensitivity			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Food allergy			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Jarisch-Herxheimer reaction			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Social circumstances			
Bereavement			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Family stress			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Substance use			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Treatment noncompliance			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	4 / 242 (1.65%)	4 / 242 (1.65%)	0 / 123 (0.00%)
occurrences (all)	4	5	0

Prostatitis			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	4	2	0
Balanoposthitis			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Breast cyst			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	1	0	1
Genital lesion			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Penile discharge			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Varicocele			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Asthenospermia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Breast discharge			
subjects affected / exposed	0 / 242 (0.00%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	0	0	1
Breast mass			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Cervical dysplasia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Ejaculation failure			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0

Genital discomfort			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Genital rash			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Gynaecomastia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Haematospermia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Menorrhagia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Ovarian cyst			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Testicular pain			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Vaginal haemorrhage			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	19 / 242 (7.85%)	18 / 242 (7.44%)	1 / 123 (0.81%)
occurrences (all)	21	20	1
Oropharyngeal pain			
subjects affected / exposed	10 / 242 (4.13%)	10 / 242 (4.13%)	0 / 123 (0.00%)
occurrences (all)	10	10	0
Sinus congestion			

subjects affected / exposed	8 / 242 (3.31%)	6 / 242 (2.48%)	0 / 123 (0.00%)
occurrences (all)	9	8	0
Nasal congestion			
subjects affected / exposed	6 / 242 (2.48%)	4 / 242 (1.65%)	1 / 123 (0.81%)
occurrences (all)	6	7	1
Rhinitis allergic			
subjects affected / exposed	3 / 242 (1.24%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	3	3	0
Asthma			
subjects affected / exposed	4 / 242 (1.65%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	4	3	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 242 (0.00%)	4 / 242 (1.65%)	1 / 123 (0.81%)
occurrences (all)	0	4	1
Productive cough			
subjects affected / exposed	3 / 242 (1.24%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	3	3	0
Rhinorrhoea			
subjects affected / exposed	2 / 242 (0.83%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	3	3	0
Dyspnoea			
subjects affected / exposed	2 / 242 (0.83%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	2	2	0
Epistaxis			
subjects affected / exposed	0 / 242 (0.00%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	0	5	0
Pharyngeal erythema			
subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	2	0
Pulmonary congestion			
subjects affected / exposed	0 / 242 (0.00%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	0	4	0
Tonsillar hypertrophy			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0

Upper-airway cough syndrome			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	3	0
Allergic sinusitis			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Dysphonia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	1	0	1
Dyspnoea exertional			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	3	0
Respiratory tract congestion			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Adenoidal hypertrophy			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Asthmatic crisis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Emphysema			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Hypoventilation			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Laryngeal oedema			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract congestion			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0

Nasal discharge discolouration			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Nasal oedema			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Pharyngeal disorder			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Pharyngeal ulceration			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Rales			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Sinus pain			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Sneezing			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Throat irritation			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Tonsillar exudate			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Vocal cord polyp			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Vocal cord thickening			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0

Psychiatric disorders			
Insomnia			
subjects affected / exposed	16 / 242 (6.61%)	19 / 242 (7.85%)	1 / 123 (0.81%)
occurrences (all)	17	21	1
Anxiety			
subjects affected / exposed	9 / 242 (3.72%)	13 / 242 (5.37%)	1 / 123 (0.81%)
occurrences (all)	9	13	1
Depression			
subjects affected / exposed	8 / 242 (3.31%)	12 / 242 (4.96%)	0 / 123 (0.00%)
occurrences (all)	9	14	0
Abnormal dreams			
subjects affected / exposed	3 / 242 (1.24%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	3	3	0
Drug use disorder			
subjects affected / exposed	2 / 242 (0.83%)	4 / 242 (1.65%)	0 / 123 (0.00%)
occurrences (all)	2	4	0
Sleep disorder			
subjects affected / exposed	1 / 242 (0.41%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	1	3	0
Depressed mood			
subjects affected / exposed	3 / 242 (1.24%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	3	0	0
Libido decreased			
subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Nightmare			
subjects affected / exposed	0 / 242 (0.00%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	0	3	0
Panic attack			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Alcohol abuse			

subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Bipolar disorder			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Irritability			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Libido disorder			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Tobacco abuse			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Adjustment disorder			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Aggression			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Alcohol withdrawal syndrome			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Anorexia nervosa			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Burnout syndrome			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Dissociation			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Eating disorder			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Flat affect			

subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Initial insomnia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Intentional self-injury			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Loss of libido			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Middle insomnia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	0	0	1
Mood swings			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Nervousness			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Persistent depressive disorder			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Psychomotor retardation			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Stress			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Suicide attempt			
subjects affected / exposed	0 / 242 (0.00%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	0	0	1
Substance use disorder			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Tic			

subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Hepatic steatosis			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Gallbladder cholesterolosis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Hepatitis alcoholic			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Hepatosplenomegaly			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 242 (0.83%)	9 / 242 (3.72%)	0 / 123 (0.00%)
occurrences (all)	2	9	0
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 242 (1.65%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	4	2	0
Blood triglycerides increased			
subjects affected / exposed	3 / 242 (1.24%)	1 / 242 (0.41%)	1 / 123 (0.81%)
occurrences (all)	3	1	1
Weight increased			
subjects affected / exposed	2 / 242 (0.83%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	2	3	0
Blood cholesterol increased			
subjects affected / exposed	3 / 242 (1.24%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	3	3	0
Blood creatinine increased			

subjects affected / exposed	0 / 242 (0.00%)	4 / 242 (1.65%)	0 / 123 (0.00%)
occurrences (all)	0	4	0
Transaminases increased			
subjects affected / exposed	2 / 242 (0.83%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	2	2	0
Weight decreased			
subjects affected / exposed	3 / 242 (1.24%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	3	1	0
Alanine aminotransferase increased			
subjects affected / exposed	3 / 242 (1.24%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	3	0	0
Lipase increased			
subjects affected / exposed	3 / 242 (1.24%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	4	0	0
Blood phosphorus decreased			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	3	0	0
Blood testosterone decreased			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
High density lipoprotein decreased			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Blood creatine phosphokinase abnormal			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Blood creatinine abnormal			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0

Blood glucose increased			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	3	0	0
Blood urine present			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Campylobacter test positive			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Creatinine renal clearance decreased			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram repolarisation abnormality			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Lipids increased			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Liver function test increased			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Low density lipoprotein increased			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Lymph node palpable			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			

subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Neutrophil count increased			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Parasite stool test positive			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Protein urine present			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
White blood cells urine positive			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	2 / 242 (0.83%)	4 / 242 (1.65%)	0 / 123 (0.00%)
occurrences (all)	2	4	0
Procedural pain			
subjects affected / exposed	1 / 242 (0.41%)	5 / 242 (2.07%)	0 / 123 (0.00%)
occurrences (all)	1	5	0
Contusion			
subjects affected / exposed	4 / 242 (1.65%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	4	1	0
Ligament sprain			
subjects affected / exposed	1 / 242 (0.41%)	4 / 242 (1.65%)	0 / 123 (0.00%)
occurrences (all)	1	4	0
Hand fracture			
subjects affected / exposed	2 / 242 (0.83%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	3	2	0
Animal bite			
subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	3	1	0
Fall			

subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Laceration			
subjects affected / exposed	0 / 242 (0.00%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	0	3	0
Muscle strain			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Thermal burn			
subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Burn oral cavity			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Foot fracture			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	1 / 123 (0.81%)
occurrences (all)	0	1	1
Joint injury			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	1 / 123 (0.81%)
occurrences (all)	0	1	1
Ligament rupture			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Meniscus injury			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Rib fracture			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Road traffic accident			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Skin abrasion			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Tooth fracture			

subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Arthropod sting			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Axillary nerve injury			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Back injury			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Burns first degree			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Burns second degree			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Burns third degree			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Concussion			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Corneal abrasion			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Epicondylitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Eye injury			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Head injury			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Incision site haemorrhage			

subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Incision site pain			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Patella fracture			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Penis injury			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Post procedural swelling			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Post-traumatic pain			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Product use complaint			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Scrotal haematoma			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Skin injury			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Sports injury			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Sunburn			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Tendon rupture			

subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Congenital, familial and genetic disorders			
Bicuspid aortic valve			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Type V hyperlipidaemia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 242 (0.00%)	4 / 242 (1.65%)	0 / 123 (0.00%)
occurrences (all)	0	4	0
Extrasystoles			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Tachycardia			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Arrhythmia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Atrioventricular block second degree			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Bradycardia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Bundle branch block left			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Cardiac failure			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Cardiac failure congestive			

subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Myocardial infarction			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Pericarditis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Ventricular hypertrophy			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	26 / 242 (10.74%)	40 / 242 (16.53%)	2 / 123 (1.63%)
occurrences (all)	29	45	2
Dizziness			
subjects affected / exposed	13 / 242 (5.37%)	14 / 242 (5.79%)	0 / 123 (0.00%)
occurrences (all)	14	15	0
Hypoaesthesia			
subjects affected / exposed	2 / 242 (0.83%)	4 / 242 (1.65%)	0 / 123 (0.00%)
occurrences (all)	2	4	0
Paraesthesia			
subjects affected / exposed	4 / 242 (1.65%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	5	1	0
Sciatica			
subjects affected / exposed	0 / 242 (0.00%)	4 / 242 (1.65%)	1 / 123 (0.81%)
occurrences (all)	0	4	1
Somnolence			
subjects affected / exposed	3 / 242 (1.24%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	3	2	0
Migraine			
subjects affected / exposed	4 / 242 (1.65%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	4	0	0
Balance disorder			
subjects affected / exposed	3 / 242 (1.24%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	3	0	0

Memory impairment			
subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Syncope			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Dysgeusia			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Burning sensation			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Cervicobrachial syndrome			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Disturbance in attention			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Dysarthria			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Facial paralysis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Lethargy			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Lumbar radiculopathy			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Mental impairment			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0

Nerve compression			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Post herpetic neuralgia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Sinus headache			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	6 / 242 (2.48%)	7 / 242 (2.89%)	0 / 123 (0.00%)
occurrences (all)	6	7	0
Neutropenia			
subjects affected / exposed	3 / 242 (1.24%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	3	3	0
Anaemia			
subjects affected / exposed	1 / 242 (0.41%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	1	3	0
Eosinophilia			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Haemorrhagic anaemia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Leukocytosis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Leukopenia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			

Ear congestion			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	3	0
Tinnitus			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	1 / 123 (0.81%)
occurrences (all)	1	3	1
Vertigo			
subjects affected / exposed	3 / 242 (1.24%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	4	0	0
Deafness			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Cerumen impaction			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Ear canal erythema			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Chalazion			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Vitreous floaters			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Cataract			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Keratitis			

subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Scleral discolouration			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Xerophthalmia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	74 / 242 (30.58%)	43 / 242 (17.77%)	2 / 123 (1.63%)
occurrences (all)	98	46	2
Nausea			
subjects affected / exposed	48 / 242 (19.83%)	40 / 242 (16.53%)	2 / 123 (1.63%)
occurrences (all)	56	45	2
Vomiting			
subjects affected / exposed	17 / 242 (7.02%)	15 / 242 (6.20%)	0 / 123 (0.00%)
occurrences (all)	22	16	0
Abdominal pain			
subjects affected / exposed	12 / 242 (4.96%)	13 / 242 (5.37%)	0 / 123 (0.00%)
occurrences (all)	12	14	0
Constipation			
subjects affected / exposed	5 / 242 (2.07%)	13 / 242 (5.37%)	0 / 123 (0.00%)
occurrences (all)	5	13	0
Abdominal distension			
subjects affected / exposed	9 / 242 (3.72%)	8 / 242 (3.31%)	0 / 123 (0.00%)
occurrences (all)	9	10	0
Haemorrhoids			
subjects affected / exposed	6 / 242 (2.48%)	8 / 242 (3.31%)	1 / 123 (0.81%)
occurrences (all)	6	8	1
Flatulence			
subjects affected / exposed	11 / 242 (4.55%)	5 / 242 (2.07%)	0 / 123 (0.00%)
occurrences (all)	11	6	0
Abdominal pain upper			
subjects affected / exposed	4 / 242 (1.65%)	10 / 242 (4.13%)	0 / 123 (0.00%)
occurrences (all)	4	10	0

Dyspepsia			
subjects affected / exposed	7 / 242 (2.89%)	5 / 242 (2.07%)	0 / 123 (0.00%)
occurrences (all)	9	6	0
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 242 (1.65%)	6 / 242 (2.48%)	0 / 123 (0.00%)
occurrences (all)	4	8	0
Abdominal discomfort			
subjects affected / exposed	6 / 242 (2.48%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	7	3	0
Rectal haemorrhage			
subjects affected / exposed	3 / 242 (1.24%)	4 / 242 (1.65%)	1 / 123 (0.81%)
occurrences (all)	3	4	1
Faeces soft			
subjects affected / exposed	3 / 242 (1.24%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	3	3	0
Anal fissure			
subjects affected / exposed	3 / 242 (1.24%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	3	2	0
Dry mouth			
subjects affected / exposed	2 / 242 (0.83%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	2	4	0
Toothache			
subjects affected / exposed	3 / 242 (1.24%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	3	2	0
Dental caries			
subjects affected / exposed	2 / 242 (0.83%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	2	2	0
Gastritis			
subjects affected / exposed	3 / 242 (1.24%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	3	1	0
Proctalgia			
subjects affected / exposed	0 / 242 (0.00%)	4 / 242 (1.65%)	0 / 123 (0.00%)
occurrences (all)	0	4	0
Aphthous ulcer			
subjects affected / exposed	0 / 242 (0.00%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	0	3	0

Colitis			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Haematochezia			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Proctitis			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Anal ulcer			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Anogenital dysplasia			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Anorectal disorder			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Enterocolitis			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Food poisoning			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Frequent bowel movements			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Oral pain			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0

Tongue coated			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Abdominal hernia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Abdominal pain lower			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Abdominal tenderness			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Anal haemorrhage			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Anal pruritus			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Anorectal discomfort			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Colitis microscopic			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Crohn's disease			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Dysphagia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0

Gastrointestinal erosion			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal inflammation			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Gingival disorder			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Gingival recession			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Glossodynia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids thrombosed			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Hyperchlorhydria			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Inguinal hernia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Intestinal polyp			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Leukoplakia oral			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Mucous stools			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0

Noninfective gingivitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Odynophagia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Oedema mouth			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Oesophagitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	0	0	1
Palatal disorder			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Pancreatitis chronic			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Rectal lesion			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Tongue disorder			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Tongue dry			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Tongue ulceration			
subjects affected / exposed	0 / 242 (0.00%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	0	0	1
Tooth impacted			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	17 / 242 (7.02%)	13 / 242 (5.37%)	0 / 123 (0.00%)
occurrences (all)	19	13	0
Pruritus			
subjects affected / exposed	7 / 242 (2.89%)	5 / 242 (2.07%)	0 / 123 (0.00%)
occurrences (all)	9	6	0
Night sweats			
subjects affected / exposed	6 / 242 (2.48%)	2 / 242 (0.83%)	1 / 123 (0.81%)
occurrences (all)	6	2	1
Alopecia			
subjects affected / exposed	1 / 242 (0.41%)	5 / 242 (2.07%)	0 / 123 (0.00%)
occurrences (all)	1	5	0
Dry skin			
subjects affected / exposed	3 / 242 (1.24%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	3	3	0
Acne			
subjects affected / exposed	1 / 242 (0.41%)	4 / 242 (1.65%)	0 / 123 (0.00%)
occurrences (all)	1	4	0
Eczema			
subjects affected / exposed	2 / 242 (0.83%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	2	3	0
Dermatitis			
subjects affected / exposed	3 / 242 (1.24%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	3	1	0
Erythema			
subjects affected / exposed	0 / 242 (0.00%)	3 / 242 (1.24%)	1 / 123 (0.81%)
occurrences (all)	0	3	1
Psoriasis			
subjects affected / exposed	4 / 242 (1.65%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	4	0	0
Rash macular			
subjects affected / exposed	2 / 242 (0.83%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	2	2	0
Seborrhoeic dermatitis			

subjects affected / exposed	4 / 242 (1.65%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	4	0	0
Urticaria			
subjects affected / exposed	3 / 242 (1.24%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	4	1	0
Dermal cyst			
subjects affected / exposed	0 / 242 (0.00%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	0	3	0
Dermatitis allergic			
subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Dermatitis contact			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Dyshidrotic eczema			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Skin lesion			
subjects affected / exposed	0 / 242 (0.00%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	0	3	0
Drug eruption			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Pruritus generalised			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Seborrhoea			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Alopecia areata			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Blister			

subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Cold sweat			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Dermatosis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Guttate psoriasis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Hair colour changes			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Hand dermatitis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Hyperkeratosis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Intertrigo			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Lipodystrophy acquired			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Miliaria			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Mucocutaneous ulceration			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Penile ulceration			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Pityriasis			

subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Prurigo			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Rash erythematous			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Rash generalised			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Rash morbilliform			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Rash pruritic			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Rosacea			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Skin disorder			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Skin erosion			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Skin exfoliation			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Skin fissures			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Swelling face			

subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	3 / 242 (1.24%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	3	3	0
Nephrolithiasis			
subjects affected / exposed	2 / 242 (0.83%)	2 / 242 (0.83%)	1 / 123 (0.81%)
occurrences (all)	3	2	1
Chromaturia			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Haematuria			
subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Pollakiuria			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Renal colic			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	2 / 123 (1.63%)
occurrences (all)	2	0	2
Acute kidney injury			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	1 / 123 (0.81%)
occurrences (all)	0	1	1
Renal tubular dysfunction			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	1 / 123 (0.81%)
occurrences (all)	0	1	1
Urine flow decreased			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Bladder disorder			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Micturition disorder			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0

Micturition urgency			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Renal failure			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Urethral discharge			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Urinary hesitation			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hypogonadism			
subjects affected / exposed	2 / 242 (0.83%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	2	2	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	17 / 242 (7.02%)	14 / 242 (5.79%)	0 / 123 (0.00%)
occurrences (all)	17	14	0
Arthralgia			
subjects affected / exposed	15 / 242 (6.20%)	9 / 242 (3.72%)	0 / 123 (0.00%)
occurrences (all)	19	10	0
Myalgia			
subjects affected / exposed	12 / 242 (4.96%)	7 / 242 (2.89%)	1 / 123 (0.81%)
occurrences (all)	13	7	1
Pain in extremity			
subjects affected / exposed	9 / 242 (3.72%)	9 / 242 (3.72%)	0 / 123 (0.00%)
occurrences (all)	12	9	0
Muscle spasms			

subjects affected / exposed	3 / 242 (1.24%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	3	3	0
Neck pain			
subjects affected / exposed	4 / 242 (1.65%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	4	2	0
Muscle contracture			
subjects affected / exposed	1 / 242 (0.41%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	1	3	0
Osteopenia			
subjects affected / exposed	1 / 242 (0.41%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	1	3	0
Tendonitis			
subjects affected / exposed	1 / 242 (0.41%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	1	3	0
Flank pain			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	2	2	0
Joint swelling			
subjects affected / exposed	3 / 242 (1.24%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	3	0	0
Osteoporosis			
subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Pain in jaw			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Arthritis			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Bursitis			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Groin pain			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Intervertebral disc protrusion			

subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	1 / 123 (0.81%)
occurrences (all)	0	1	1
Musculoskeletal pain			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Osteoarthritis			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Spinal disorder			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	1	0	1
Axillary mass			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Costochondritis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Fibromyalgia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Foot deformity			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Intervertebral disc disorder			
subjects affected / exposed	0 / 242 (0.00%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	0	0	1
Joint range of motion decreased			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Joint stiffness			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Metatarsalgia			

subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Rhabdomyolysis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Rotator cuff syndrome			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Tendon disorder			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Torticollis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	24 / 242 (9.92%)	26 / 242 (10.74%)	5 / 123 (4.07%)
occurrences (all)	26	33	5
Upper respiratory tract infection			
subjects affected / exposed	27 / 242 (11.16%)	16 / 242 (6.61%)	1 / 123 (0.81%)
occurrences (all)	30	22	1
Bronchitis			
subjects affected / exposed	17 / 242 (7.02%)	12 / 242 (4.96%)	0 / 123 (0.00%)
occurrences (all)	20	12	0
Gastroenteritis			
subjects affected / exposed	14 / 242 (5.79%)	12 / 242 (4.96%)	3 / 123 (2.44%)
occurrences (all)	16	13	3

Pharyngitis			
subjects affected / exposed	14 / 242 (5.79%)	11 / 242 (4.55%)	1 / 123 (0.81%)
occurrences (all)	15	11	1
Syphilis			
subjects affected / exposed	12 / 242 (4.96%)	11 / 242 (4.55%)	2 / 123 (1.63%)
occurrences (all)	12	12	2
Sinusitis			
subjects affected / exposed	13 / 242 (5.37%)	9 / 242 (3.72%)	0 / 123 (0.00%)
occurrences (all)	14	10	0
Influenza			
subjects affected / exposed	11 / 242 (4.55%)	4 / 242 (1.65%)	2 / 123 (1.63%)
occurrences (all)	11	4	2
Folliculitis			
subjects affected / exposed	6 / 242 (2.48%)	7 / 242 (2.89%)	0 / 123 (0.00%)
occurrences (all)	6	7	0
Urethritis			
subjects affected / exposed	4 / 242 (1.65%)	8 / 242 (3.31%)	1 / 123 (0.81%)
occurrences (all)	4	8	1
Conjunctivitis			
subjects affected / exposed	7 / 242 (2.89%)	4 / 242 (1.65%)	1 / 123 (0.81%)
occurrences (all)	7	4	1
Gonorrhoea			
subjects affected / exposed	4 / 242 (1.65%)	8 / 242 (3.31%)	0 / 123 (0.00%)
occurrences (all)	4	9	0
Rhinitis			
subjects affected / exposed	6 / 242 (2.48%)	4 / 242 (1.65%)	1 / 123 (0.81%)
occurrences (all)	8	4	1
Urinary tract infection			
subjects affected / exposed	4 / 242 (1.65%)	7 / 242 (2.89%)	0 / 123 (0.00%)
occurrences (all)	5	7	0
Tonsillitis			
subjects affected / exposed	3 / 242 (1.24%)	5 / 242 (2.07%)	1 / 123 (0.81%)
occurrences (all)	4	5	1
Oral herpes			
subjects affected / exposed	2 / 242 (0.83%)	6 / 242 (2.48%)	0 / 123 (0.00%)
occurrences (all)	2	6	0

Respiratory tract infection			
subjects affected / exposed	5 / 242 (2.07%)	2 / 242 (0.83%)	1 / 123 (0.81%)
occurrences (all)	5	3	1
Furuncle			
subjects affected / exposed	4 / 242 (1.65%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	5	3	0
Herpes zoster			
subjects affected / exposed	5 / 242 (2.07%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	5	2	0
Nasopharyngitis			
subjects affected / exposed	2 / 242 (0.83%)	3 / 242 (1.24%)	2 / 123 (1.63%)
occurrences (all)	2	3	2
Tooth abscess			
subjects affected / exposed	5 / 242 (2.07%)	1 / 242 (0.41%)	1 / 123 (0.81%)
occurrences (all)	7	1	1
Viral infection			
subjects affected / exposed	1 / 242 (0.41%)	6 / 242 (2.48%)	0 / 123 (0.00%)
occurrences (all)	1	6	0
Acarodermatitis			
subjects affected / exposed	1 / 242 (0.41%)	5 / 242 (2.07%)	0 / 123 (0.00%)
occurrences (all)	1	5	0
Chlamydial infection			
subjects affected / exposed	3 / 242 (1.24%)	2 / 242 (0.83%)	1 / 123 (0.81%)
occurrences (all)	3	2	1
Fungal skin infection			
subjects affected / exposed	4 / 242 (1.65%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	5	2	0
Tooth infection			
subjects affected / exposed	5 / 242 (2.07%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	5	1	0
Gastroenteritis viral			
subjects affected / exposed	1 / 242 (0.41%)	3 / 242 (1.24%)	1 / 123 (0.81%)
occurrences (all)	1	3	1
Cellulitis			
subjects affected / exposed	0 / 242 (0.00%)	4 / 242 (1.65%)	0 / 123 (0.00%)
occurrences (all)	0	4	0

Fungal infection			
subjects affected / exposed	2 / 242 (0.83%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	2	2	0
Genital herpes			
subjects affected / exposed	1 / 242 (0.41%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	1	4	0
Gingivitis			
subjects affected / exposed	2 / 242 (0.83%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	2	2	0
Hordeolum			
subjects affected / exposed	3 / 242 (1.24%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	4	1	0
Herpes simplex			
subjects affected / exposed	0 / 242 (0.00%)	4 / 242 (1.65%)	0 / 123 (0.00%)
occurrences (all)	0	4	0
Tinea pedis			
subjects affected / exposed	3 / 242 (1.24%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	3	1	0
Abscess			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Abscess limb			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	2	2	0
Body tinea			
subjects affected / exposed	0 / 242 (0.00%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	0	3	0
Dermatophytosis			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	2	2	0
Ear infection			
subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Herpes virus infection			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	2	2	0

Lower respiratory tract infection			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Onychomycosis			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	1 / 123 (0.81%)
occurrences (all)	0	2	1
Oral fungal infection			
subjects affected / exposed	3 / 242 (1.24%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	3	0	0
Pharyngitis streptococcal			
subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Pneumonia			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Staphylococcal infection			
subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Abdominal abscess			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Acute sinusitis			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Anal abscess			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Anal chlamydia infection			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Cystitis			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Ear infection fungal			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0

Hepatitis C			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Infected bite			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Latent tuberculosis			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Molluscum contagiosum			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Oral candidiasis			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Papilloma viral infection			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Paronychia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	1 / 123 (0.81%)
occurrences (all)	0	1	1
Proctitis gonococcal			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Periodontitis			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	3	0
Rash pustular			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Respiratory tract infection viral			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	2	0	1

Secondary syphilis			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Subcutaneous abscess			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Tinea cruris			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Tinea versicolour			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Trichomoniasis			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Urethritis chlamydial			
subjects affected / exposed	1 / 242 (0.41%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	1	1	0
Urethritis gonococcal			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	1 / 123 (0.81%)
occurrences (all)	0	1	1
Viral rhinitis			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Viral rash			
subjects affected / exposed	0 / 242 (0.00%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Vulvovaginal candidiasis			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	2	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	2 / 242 (0.83%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	3	0	0
Anal infection			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0

Bacterial vaginosis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Borrelia infection			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Bronchitis viral			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Carbuncle			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Chronic sinusitis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Chronic tonsillitis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Condyloma latum			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Diarrhoea infectious			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Empyema			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Enterobiasis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0

Escherichia urinary tract infection			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Eye infection syphilitic			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Genital candidiasis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Genitourinary chlamydia infection			
subjects affected / exposed	0 / 242 (0.00%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	0	0	1
Groin abscess			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Helicobacter gastritis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Infected fistula			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Infection			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Labyrinthitis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Laryngitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Latent syphilis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Localised infection			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0

Orchitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Oropharyngitis fungal			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Osteomyelitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Otitis externa			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Parotitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Peritonsillar abscess			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Pertussis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Primary syphilis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Proctitis chlamydial			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Pulmonary tuberculosis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0

Pyelonephritis acute			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	2	0
Rotavirus infection			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Salmonellosis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Shigella infection			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Sialoadenitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Skin candida			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Strongyloidiasis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Superinfection bacterial			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Tinea capitis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Tongue fungal infection			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Tonsillitis bacterial			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Tracheitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	0	0	1

Ureaplasma infection			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Viral pharyngitis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Wound infection staphylococcal			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 242 (3.31%)	4 / 242 (1.65%)	0 / 123 (0.00%)
occurrences (all)	8	4	0
Vitamin D deficiency			
subjects affected / exposed	5 / 242 (2.07%)	5 / 242 (2.07%)	0 / 123 (0.00%)
occurrences (all)	5	5	0
Dyslipidaemia			
subjects affected / exposed	4 / 242 (1.65%)	3 / 242 (1.24%)	0 / 123 (0.00%)
occurrences (all)	4	4	0
Hyperlipidaemia			
subjects affected / exposed	5 / 242 (2.07%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	5	1	0
Hypercholesterolaemia			
subjects affected / exposed	5 / 242 (2.07%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	5	0	0
Hypertriglyceridaemia			
subjects affected / exposed	3 / 242 (1.24%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	3	0	1
Hyponatraemia			
subjects affected / exposed	1 / 242 (0.41%)	2 / 242 (0.83%)	0 / 123 (0.00%)
occurrences (all)	1	2	0
Hypophosphataemia			

subjects affected / exposed	2 / 242 (0.83%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	2	1	0
Abnormal loss of weight			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Abnormal weight gain			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Dehydration			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Diabetes mellitus			
subjects affected / exposed	0 / 242 (0.00%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	0	0	1
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Gout			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 242 (0.00%)	1 / 123 (0.81%)
occurrences (all)	0	0	1
Hyperlipasaemia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Hypovolaemia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Iron deficiency			

subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Lipid metabolism disorder			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Obesity			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 242 (0.00%)	1 / 242 (0.41%)	0 / 123 (0.00%)
occurrences (all)	0	1	0
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 242 (0.41%)	0 / 242 (0.00%)	0 / 123 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 August 2011	• Addition of Child-Pugh classification to the Time and Events table. • Addition of Rash toxicity as a study withdrawal criterion. • EudraCT number correction. • Use of Health Outcomes instruments only in countries where translations are available. • Addition of an electrocardiogram (ECG) at Week 48. • Addition of the PSRAE form • Addition of information regarding rash associated with DTG. • Addition of text regarding the snapshot algorithm and switching of background regimen and update to study results availability.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported