Clinical trial results:
An Open-Label, Phase 3 Study of Telaprevir in Combination With Peginterferon Alfa-2a (Pegasys®) and Ribavirin (Copegus®) in Subjects Coinfected With Genotype 1 Hepatitis C Virus and Human Immunodeficiency Virus Type 1(HCV/HIV-1)

Summary

EudraCT number	2011-002668-25
Trial protocol	DE ES
Global end of trial date	04 February 2014

Results information

Result version number	v1 (current)
This version publication date	28 June 2016
First version publication date	07 August 2015

Trial information

Trial identification

Sponsor protocol code	VX11-950-115

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01467479
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vertex Pharmaceuticals Incorporated
Sponsor organisation address	50 Northern Avenue, Boston, Massachusetts, United States, 02210-1862
Public contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, 1 617-341-6777, medicalinfo@vrtx.com
Scientific contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, 1 617-341-6777, medicalinfo@vrtx.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 February 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 February 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to evaluate the antiviral efficacy of response-guided dosing of telaprevir, peginterferon alfa-2a (Peg-IFN-alfa-2a), and ribavarin during 24 or 48-week treatment in subjects co-infected with human immunodeficiency virus (HIV) and Hepatitis C Virus (HCV), who were treatment-naive for HCV or received prior HCV treatment with Peg-IFN-alfa-2a and ribavirin and experienced viral relapse.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 December 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	United States: 144
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Spain: 15
Worldwide total number of subjects	182
EEA total number of subjects	22

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)	179
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study included Treatment-Naïve (no prior hepatitis C virus [HCV] therapy); Prior Relapser (prior HCV treatment with Peg-IFN/RBV and experienced viral relapse); and Prior Null/Partial Responder (prior HCV treatment with Peg-IFN/RBV and had null/partial response) subjects.

Pre-assignment

Screening details:

Total 55, 69, and 61 subjects were enrolled in "T/PR + HAART Regimen (ATV/r-Based)", "T/PR + HAART Regimen (EFV-Based)" and "T/PR + HAART Regimen (RAL-Based)" arms, respectively of which 54, 69, and 59 subjects were treated. Results were reported as per HAART treatment and also separately as per prior response, unless otherwise specified.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	T/PR + HAART Regimen (ATV/r-Based)

Arm description:

Subjects who were receiving atazanavir/ritonavir (ATV/r) based Highly Active Antiretroviral Therapy (HAART) at baseline, received Telaprevir (T) 1125 milligram (mg) tablet twice daily for 12 weeks in combination with pegylated interferon alfa 2a (P) (Peg-IFN-alfa-2a) 180 microgram per week (mcg/week) subcutaneous injection and ribavirin (R) (RBV) tablet orally twice daily at a dose of 800 milligram per day (mg/day) for 24 or 48 weeks, depending on individual response to telaprevir treatment. Subjects continued their HAART, as per standard practice and investigator discretion.

Arm type	Experimental
Investigational medicinal product name	Telaprevir
Investigational medicinal product code	VX-950
Other name	Incivek
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Telaprevir 1125 mg tablet twice daily for 12 weeks.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Copegus®, RBV
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin (RBV) tablet twice daily at a dose of 800 mg/day for 24 or 48 weeks.

Investigational medicinal product name	Pegylated Interferon Alfa-2a
Investigational medicinal product code	
Other name	Pegasys®, Peg-IFN-Alfa-2a
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Peg-IFN-alfa-2a 180 mcg/week subcutaneous injection.

Investigational medicinal product name	Atazanavir/ritonavir (ATV/r)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Capsule, soft, Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Atazanavir/ritonavir (ATV/r) based HAART as per standard practice.

Arm title	T/PR + HAART Regimen (EFV-Based)

Arm description:

Subjects who were receiving efavirenz (EFV) based HAART at baseline, received Telaprevir 1125 mg tablet three times a day for 12 weeks in combination with Peg-IFN-alfa-2a 180 mcg/week subcutaneous injection and RBV tablet orally twice daily at a dose of 800 mg/day for 24 or 48 weeks, depending on individual response to telaprevir treatment. Subjects continued their HAART, as per standard practice and investigator discretion.

Arm type	Experimental
Investigational medicinal product name	Telaprevir
Investigational medicinal product code	VX-950
Other name	Incivek
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Telaprevir 1125 mg tablet three times a day for 12 weeks.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Copegus®, RBV
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin tablet twice daily at a dose of 800 mg/day for 24 or 48 weeks.

Investigational medicinal product name	Pegylated Interferon Alfa-2a
Investigational medicinal product code	
Other name	Pegasys®, Peg-IFN-Alfa-2a
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Pegylated interferon alfa 2a 180 mcg/week subcutaneous injection.

Investigational medicinal product name	Efavirenz (EFV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Efavirenz based HAART as per standard practice.

Arm title	T/PR + HAART Regimen (RAL-Based)

Arm description:

Subjects who were receiving raltegravir (RAL) based HAART at baseline, received Telaprevir 1125 mg tablet twice daily for 12 weeks in combination with Peg-IFN-alfa-2a 180 mcg/week subcutaneous injection and RBV tablet orally twice daily at a dose of 800 mg/day for 24 or 48 weeks, depending on individual response to telaprevir treatment. Subjects continued their HAART, as per standard practice and investigator discretion.

Arm type	Experimental

Investigational medicinal product name	Telaprevir
Investigational medicinal product code	VX-950
Other name	Incivek
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Telaprevir 1125 mg tablet twice daily for 12 weeks.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Copegus®, RBV
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin tablet twice daily at a dose of 800 mg/day for 24 or 48 weeks.

Investigational medicinal product name	Pegylated Interferon Alfa-2a
Investigational medicinal product code	
Other name	Pegasys®, Peg-IFN-Alfa-2a
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Peg-IFN-alfa-2a 180 mcg/week subcutaneous injection.

Investigational medicinal product name	Raltegravir (RAL)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral suspension, Tablet
Routes of administration	Oral use

Dosage and administration details:

Raltegravir based HAART as per standard practice.

Number of subjects in period 1	T/PR + HAART Regimen (ATV/r-Based)	T/PR + HAART Regimen (EFV-Based)	T/PR + HAART Regimen (RAL-Based)
Started	54	69	59
Completed	46	52	45
Not completed	8	17	14
Consent withdrawn by subject	3	7	7
Adverse Event	1	2	-
Death	-	-	1
Unspecified	1	-	-
Study Terminated by Sponsor	1	3	3
Lost to follow-up	2	5	3

Baseline characteristics

Reporting groups	
Reporting group title	T/PR + HAART Regimen (ATV/r-Based)

Reporting group description:

Subjects who were receiving atazanavir/ritonavir (ATV/r) based Highly Active Antiretroviral Therapy (HAART) at baseline, received Telaprevir (T) 1125 milligram (mg) tablet twice daily for 12 weeks in combination with pegylated interferon alfa 2a (P) (Peg-IFN-alfa-2a) 180 microgram per week (mcg/week) subcutaneous injection and ribavirin (R) (RBV) tablet orally twice daily at a dose of 800 milligram per day (mg/day) for 24 or 48 weeks, depending on individual response to telaprevir treatment. Subjects continued their HAART, as per standard practice and investigator discretion.

Reporting group title	T/PR + HAART Regimen (EFV-Based)

Reporting group description:

Subjects who were receiving efavirenz (EFV) based HAART at baseline, received Telaprevir 1125 mg tablet three times a day for 12 weeks in combination with Peg-IFN-alfa-2a 180 mcg/week subcutaneous injection and RBV tablet orally twice daily at a dose of 800 mg/day for 24 or 48 weeks, depending on individual response to telaprevir treatment. Subjects continued their HAART, as per standard practice and investigator discretion.

Reporting group title	T/PR + HAART Regimen (RAL-Based)

Reporting group description:

Subjects who were receiving raltegravir (RAL) based HAART at baseline, received Telaprevir 1125 mg tablet twice daily for 12 weeks in combination with Peg-IFN-alfa-2a 180 mcg/week subcutaneous injection and RBV tablet orally twice daily at a dose of 800 mg/day for 24 or 48 weeks, depending on individual response to telaprevir treatment. Subjects continued their HAART, as per standard practice and investigator discretion.

Reporting group values	T/PR + HAART Regimen (ATV/r-Based)	T/PR + HAART Regimen (EFV-Based)	T/PR + HAART Regimen (RAL-Based)
Number of subjects	54	69	59
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	50.4	49.6	48.4
standard deviation	± 8.81	± 8.84	± 9.58
Gender categorical Units: Subjects			
Female	6	9	15
Male	48	60	44

Reporting group values	Total		
Number of subjects	182		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean			
standard deviation	-		

Gender categorical Units: Subjects			
Female	30		
Male	152		

End points

End points reporting groups

Reporting group title	T/PR + HAART Regimen (ATV/r-Based)

Reporting group description:

Subjects who were receiving atazanavir/ritonavir (ATV/r) based Highly Active Antiretroviral Therapy (HAART) at baseline, received Telaprevir (T) 1125 milligram (mg) tablet twice daily for 12 weeks in combination with pegylated interferon alfa 2a (P) (Peg-IFN-alfa-2a) 180 microgram per week (mcg/week) subcutaneous injection and ribavirin (R) (RBV) tablet orally twice daily at a dose of 800 milligram per day (mg/day) for 24 or 48 weeks, depending on individual response to telaprevir treatment. Subjects continued their HAART, as per standard practice and investigator discretion.

Reporting group title	T/PR + HAART Regimen (EFV-Based)

Reporting group description:

Subjects who were receiving efavirenz (EFV) based HAART at baseline, received Telaprevir 1125 mg tablet three times a day for 12 weeks in combination with Peg-IFN-alfa-2a 180 mcg/week subcutaneous injection and RBV tablet orally twice daily at a dose of 800 mg/day for 24 or 48 weeks, depending on individual response to telaprevir treatment. Subjects continued their HAART, as per standard practice and investigator discretion.

Reporting group title	T/PR + HAART Regimen (RAL-Based)

Reporting group description:

Subjects who were receiving raltegravir (RAL) based HAART at baseline, received Telaprevir 1125 mg tablet twice daily for 12 weeks in combination with Peg-IFN-alfa-2a 180 mcg/week subcutaneous injection and RBV tablet orally twice daily at a dose of 800 mg/day for 24 or 48 weeks, depending on individual response to telaprevir treatment. Subjects continued their HAART, as per standard practice and investigator discretion.

Subject analysis set title	T/PR + HAART Regimen
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who were receiving either ATV/r based HAART or EFV based HAART or RAL based HAART at baseline, received Telaprevir 1125 mg tablet twice daily or 1125 mg three times a day for 12 weeks in combination with Peg-IFN-alfa-2a 180 mcg/week subcutaneous injection and RBV tablet orally twice daily at a dose of 800 mg/day for 24 or 48 weeks, depending on individual response to telaprevir treatment. Subjects continued their respective HAART, as per standard practice and investigator discretion.

Primary: Percentage of Subjects With Sustained Viral Response 12 Weeks After Last Planned Dose of Study Drug (SVR12)

End point title	Percentage of Subjects With Sustained Viral Response 12 Weeks After Last Planned Dose of Study Drug (SVR12)[1]

End point description:

SVR 12 was defined as an undetectable Hepatitis C Virus (HCV) Ribonucleic Acid (RNA) Levels (<lower limit of quantification) at 12 weeks after last planned dose of study drug. The plasma hepatitis C virus ribonucleic acid (HCV RNA) level was measured using Roche TaqMan HCV RNA assay. The lower limit of quantification was 25 international units per milliliter (IU/mL). Analysis was carried out on safety set defined as all subjects who received at least 1 dose of study drug. Here, n = subjects evaluable for specified category for each arm, respectively.

End point type	Primary

End point timeframe:

12 weeks after last planned dose of study drug (up to Week 60)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistics was planned for this study.

End point values	T/PR + HAART Regimen (ATV/r-Based)	T/PR + HAART Regimen (EFV-Based)	T/PR + HAART Regimen (RAL-Based)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	69	59	
Units: Percentage of Subjects				
number (not applicable)				
Treatment Naïve (n= 24, 39, 31)	66.7	59	61.3	
Prior Relapser (n=8, 11, 4)	75	54.5	100	
Prior Null Responder (n= 15, 11, 15)	40	36.4	40	
Prior Partial Responder (n= 7, 8, 9)	14.3	87.5	55.6	
Total (n= 54, 69, 59)	53.7	58	57.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Sustained Viral Response 24 Weeks After Last Planned Dose of Study Drug (SVR 24)

End point title	Percentage of Subjects With Sustained Viral Response 24 Weeks After Last Planned Dose of Study Drug (SVR 24)

End point description:

SVR 24 was defined as an undetectable Hepatitis C Virus (HCV) Ribonucleic Acid (RNA) Levels (<lower limit of quantification) at 24 weeks after last planned dose of study drug. The plasma HCV RNA level was measured using Roche TaqMan HCV RNA assay. The lower limit of quantification was 25 international units per milliliter (IU/mL). Analysis was carried out on safety set defined as all subjects who received at least 1 dose of study drug. Here number of subjects analyzed = subjects evaluable for this measure and n = subjects evaluable for specified categories, for each arm, respectively.

End point type	Secondary

End point timeframe:

24 weeks after last planned dose of study drug (up to Week 72)

End point values	T/PR + HAART Regimen (ATV/r-Based)	T/PR + HAART Regimen (EFV-Based)	T/PR + HAART Regimen (RAL-Based)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	66	56	
Units: Percentage of Subjects				
number (not applicable)				
Treatment Naïve (n= 23, 38, 29)	65.2	57.9	51.7	
Prior Relapser (n=8, 11, 4)	75	54.5	100	
Prior Null Responder (n= 15, 9, 14)	33.3	22.2	35.7	
Prior Partial Responder (n= 7, 8, 9)	14.3	75	55.6	
Total (n= 53, 66, 56)	50.9	54.5	51.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Rapid Viral Response (RVR)

End point title	Percentage of Subjects With Rapid Viral Response (RVR)

End point description:

The plasma HCV RNA level was measured using Roche TaqMan HCV RNA assay. The lower limit of quantification was 25 IU/mL. RVR was defined as undetectable HCV RNA (<lower limit of quantification) 4 weeks after the start of study treatment. Analysis was carried out on safety set defined as all subjects who received at least 1 dose of study drug. Here, n = subjects evaluable for specified category for each arm, respectively.

End point type	Secondary

End point timeframe:

Week 4

End point values	T/PR + HAART Regimen (ATV/r-Based)	T/PR + HAART Regimen (EFV-Based)	T/PR + HAART Regimen (RAL-Based)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	69	59	
Units: Percentage of Subjects				
number (not applicable)				
Treatment Naïve (n= 24, 39, 31)	50	53.8	74.2	
Prior Relapser (n=8, 11, 4)	62.5	72.7	100	
Prior Null Responder (n= 15, 11, 15)	26.7	54.5	53.3	
Prior Partial Responder (n= 7, 8, 9)	42.9	50	44.4	
Total (n= 54, 69, 59)	44.4	56.5	66.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Extended Rapid Viral Response (eRVR)

End point title	Percentage of Subjects With Extended Rapid Viral Response (eRVR)

End point description:

The plasma HCV RNA level was measured using Roche TaqMan HCV RNA assay. The lower limit of quantification was 25 IU/mL. eRVR was defined as undetectable HCV RNA (<lower limit of quantification) at both 4 weeks and 12 weeks after the start of study treatment. Analysis was carried out on safety set defined as all subjects who received at least 1 dose of study drug. Here, n = subjects evaluable for specified category for each arm, respectively.

End point type	Secondary

End point timeframe:

Week 4, Week 12

End point values	T/PR + HAART Regimen (ATV/r-Based)	T/PR + HAART Regimen (EFV-Based)	T/PR + HAART Regimen (RAL-Based)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	69	59	
Units: Percentage of Subjects				
number (not applicable)				
Treatment Naïve (n= 24, 39, 31)	50	53.8	61.3	
Prior Relapser (n=8, 11, 4)	62.5	72.7	100	
Prior Null Responder (n= 15, 11, 15)	26.7	54.5	53.3	
Prior Partial Responder (n= 7, 8, 9)	14.3	50	44.4	
Total (n= 54, 69, 59)	40.7	56.5	59.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Undetectable HCV RNA at End of Treatment (EOT)

End point title	Percentage of Subjects With Undetectable HCV RNA at End of Treatment (EOT)

End point description:

The plasma HCV RNA level was measured using Roche TaqMan HCV RNA assay. The lower limit of quantification was 25 IU/mL. Percentage of subjects with undetectable HCV RNA (<lower limit of quantification) at EOT (up to Week 48) was reported. Data for this outcome was not planned to be reported by prior response. Analysis was carried out on full analysis set (FAS) population defined as all subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

EOT (up to Week 48)

End point values	T/PR + HAART Regimen (ATV/r-Based)	T/PR + HAART Regimen (EFV-Based)	T/PR + HAART Regimen (RAL-Based)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	69	59	
Units: Percentage of Subjects				
number (not applicable)	55.6	63.8	61	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Percentage of Subjects With Adverse Events (AEs) and Serious

	Adverse Events (SAEs)

End point description:

AE: any untoward medical occurrence in a subject during the study; the event does not necessarily have a causal relationship with the treatment. This includes any newly occurring event or previous condition that has increased in severity or frequency after the informed consent form is signed. SAE (subset of AE): medical event or condition, which falls into any of the following categories, regardless of its relationship to the study drug: death, life threatening adverse experience, in-patient hospitalization/prolongation of hospitalization, persistent/significant disability or incapacity, congenital anomaly/birth defect, important medical event. Analysis was carried out on safety set defined as all subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	T/PR + HAART Regimen (ATV/r-Based)	T/PR + HAART Regimen (EFV-Based)	T/PR + HAART Regimen (RAL-Based)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	69	59	
Units: Percentage of Subjects				
number (not applicable)				
AEs	100	95.7	94.9	
SAEs	13	11.6	15.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum (Cmax), Minimum (Cmin), and Average Plasma Concentration (Cavg)

End point title	Maximum (Cmax), Minimum (Cmin), and Average Plasma Concentration (Cavg)

End point description:

Cmax, Cmin, and Cavg were reported for atazanavir (ATV), efavirenz (EFV), raltegravir (RAL), and telaprevir. Analysis was carried out on FAS population defined as all subjects who received at least 1 dose of study drug. Here, n = subjects evaluable for specified category for each arm, respectively. Value 99999 represents data not available as no subject was evaluable for this parameter from the specified reporting group.

End point type	Secondary

End point timeframe:

Day -14 to Day -1 and Week 1 for ATV, EFV, and RAL; Week 1 for telaprevir

End point values	T/PR + HAART Regimen (ATV/r-Based)	T/PR + HAART Regimen (EFV-Based)	T/PR + HAART Regimen (RAL-Based)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	69	59	
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
ATV: Day -14 to Day -1, Cmax(n=46, 0, 0)	2870 (± 1580)	99999 (± 99999)	99999 (± 99999)	
ATV: Day -14 to Day -1, Cmin(n=46, 0, 0)	991 (± 635)	99999 (± 99999)	99999 (± 99999)	
ATV: Day -14 to Day -1, Cavg(n=41, 0, 0)	1100 (± 647)	99999 (± 99999)	99999 (± 99999)	
ATV: Week 1, Cmax (n=42, 0, 0)	2820 (± 1570)	99999 (± 99999)	99999 (± 99999)	
ATV: Week 1, Cmin (n=42, 0, 0)	1280 (± 636)	99999 (± 99999)	99999 (± 99999)	
ATV: Week 1, Cavg (n=30, 0, 0)	1320 (± 685)	99999 (± 99999)	99999 (± 99999)	
EFV: Day -14 to Day -1, Cmax(n=0, 60, 0)	99999 (± 99999)	3800 (± 2600)	99999 (± 99999)	
EFV: Day -14 to Day -1, Cmin(n=0, 60, 0)	99999 (± 99999)	2560 (± 1900)	99999 (± 99999)	
EFV: Day -14 to Day -1, Cavg(n=0, 51, 0)	99999 (± 99999)	2150 (± 1680)	99999 (± 99999)	
EFV: Week 1, Cmax (n=0, 51, 0)	99999 (± 99999)	3340 (± 2450)	99999 (± 99999)	
EFV: Week 1, Cmin (n=0, 51, 0)	99999 (± 99999)	2290 (± 1880)	99999 (± 99999)	
EFV: Week 1, Cavg (n=0, 47, 0)	99999 (± 99999)	1920 (± 1400)	99999 (± 99999)	
RAL: Day -14 to Day -1, Cmax(n=0, 0, 52)	99999 (± 99999)	99999 (± 99999)	1900 (± 1880)	
RAL: Day -14 to Day -1, Cmin(n=0, 0, 52)	99999 (± 99999)	99999 (± 99999)	196 (± 198)	
RAL: Day -14 to Day -1, Cavg(n=0, 0, 35)	99999 (± 99999)	99999 (± 99999)	483 (± 429)	
RAL: Week 1, Cmax (n=0, 0, 49)	99999 (± 99999)	99999 (± 99999)	2320 (± 1970)	
RAL: Week 1, Cmin (n=0, 0, 49)	99999 (± 99999)	99999 (± 99999)	281 (± 435)	
RAL: Week 1, Cavg (n=0, 0, 34)	99999 (± 99999)	99999 (± 99999)	643 (± 539)	
Telaprevir: Week 1, Cmax(n=49, 59, 54)	3160 (± 1180)	3780 (± 1670)	3470 (± 868)	
Telaprevir: Week 1, Cmin(n=49, 59, 54)	1650 (± 863)	1750 (± 961)	1840 (± 741)	
Telaprevir: Week 1, Cavg(n=30, 32, 26)	2320 (± 907)	2430 (± 1290)	2520 (± 643)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Telaprevir Resistant HCV Variant at Non-Structural Viral Protein 3-4A (NS3-4A) Region

End point title	Number of Subjects With Telaprevir Resistant HCV Variant at Non-Structural Viral Protein 3-4A (NS3-4A) Region

End point description:

Sequence analysis of the HCV NS3-4A region was performed to monitor telaprevir-resistant variants. HCV RNA was isolated from the plasma, amplified by reverse transcription-polymerase chain reaction (RT-PCR), and sequenced (sequencing assay limit of detection HCV RNA >=1000 IU/mL). Results of this outcome measure were to be reported for overall subjects instead of by HAART treatment. Analysis was carried out on FAS population defined as all subjects who received at least 1 dose of study drug. Here number of subjects analyzed = subjects who were evaluable for this measure and n = subjects evaluable for specified categories.

End point type	Secondary

End point timeframe:

Baseline, follow-up (Week 96)

End point values	T/PR + HAART Regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	180			
Units: subjects				
Baseline (n = 180)	2			
Follow-up (n = 26)	11			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 52

Adverse event reporting additional description:

Adverse events were planned to be reported as per HAART treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	T/PR + HAART Regimen (ATV/r-Based)

Reporting group description:

Subjects who were receiving atazanavir/ritonavir (ATV/r) based Highly Active Antiretroviral Therapy (HAART) at baseline, received Telaprevir (T)1125 milligram (mg) tablet twice daily for 12 weeks in combination with pegylated interferon alfa 2a (P) (Peg-IFN-alfa-2a) 180 microgram per week (mcg/week) subcutaneous injection and ribavirin (R) (RBV) tablet orally twice daily at a dose of 800 milligram per day (mg/day) for 24 or 48 weeks, depending on individual response to telaprevir treatment. Subjects continued their HAART, as per standard practice and investigator discretion.

Reporting group title	T/PR + HAART Regimen (EFV-Based)

Reporting group description:

Subjects who were receiving efavirenz (EFV) based HAART at baseline, received Telaprevir 1125 mg tablet three times a day for 12 weeks in combination with Peg-IFN-alfa-2a 180 mcg/week subcutaneous injection and RBV tablet orally twice daily at a dose of 800 mg/day for 24 or 48 weeks, depending on individual response to telaprevir treatment. Subjects continued their HAART, as per standard practice and investigator discretion.

Reporting group title	T/PR + HAART Regimen (RAL-Based)

Reporting group description:

Subjects who were receiving raltegravir (RAL) based HAART at baseline, received Telaprevir 1125 mg tablet twice daily for 12 weeks in combination with Peg-IFN-alfa-2a 180 mcg/week subcutaneous injection and RBV tablet orally twice daily at a dose of 800 mg/day for 24 or 48 weeks, depending on individual response to telaprevir treatment. Subjects continued their HAART, as per standard practice and investigator discretion.

Serious adverse events	T/PR + HAART Regimen (ATV/r-Based)	T/PR + HAART Regimen (EFV-Based)	T/PR + HAART Regimen (RAL-Based)
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 54 (12.96%)	8 / 69 (11.59%)	9 / 59 (15.25%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration			

site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (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
Pneumonitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (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
Pulmonary embolism			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (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
Injury, poisoning and procedural complications			
Clavicle fracture			

subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (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			
Syncope			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 54 (0.00%)	3 / 69 (4.35%)	4 / 59 (6.78%)
occurrences causally related to treatment / all	0 / 0	3 / 3	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinopathy			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (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
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mallory-Weiss syndrome			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (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
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin lesion			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal cyst			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			

Basedow's disease			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (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
Rhabdomyolysis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (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
Infections and infestations			
Escherichia urinary tract infection			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (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			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoas abscess			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (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
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (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

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

Non-serious adverse events	T/PR + HAART Regimen (ATV/r-Based)	T/PR + HAART Regimen (EFV-Based)	T/PR + HAART Regimen (RAL-Based)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 54 (100.00%)	66 / 69 (95.65%)	56 / 59 (94.92%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Flushing			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Peripheral coldness			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Thrombosis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	26 / 54 (48.15%)	36 / 69 (52.17%)	30 / 59 (50.85%)
occurrences (all)	32	43	34
Influenza like illness			
subjects affected / exposed	5 / 54 (9.26%)	8 / 69 (11.59%)	8 / 59 (13.56%)
occurrences (all)	5	9	8
Pyrexia			
subjects affected / exposed	9 / 54 (16.67%)	5 / 69 (7.25%)	7 / 59 (11.86%)
occurrences (all)	10	5	7
Chills			
subjects affected / exposed	8 / 54 (14.81%)	6 / 69 (8.70%)	4 / 59 (6.78%)
occurrences (all)	8	6	5
Asthenia			
subjects affected / exposed	6 / 54 (11.11%)	2 / 69 (2.90%)	9 / 59 (15.25%)
occurrences (all)	6	2	9
Injection site reaction			
subjects affected / exposed	1 / 54 (1.85%)	9 / 69 (13.04%)	4 / 59 (6.78%)
occurrences (all)	1	9	4
Irritability			

subjects affected / exposed	2 / 54 (3.70%)	5 / 69 (7.25%)	7 / 59 (11.86%)
occurrences (all)	2	6	8
Pain			
subjects affected / exposed	6 / 54 (11.11%)	2 / 69 (2.90%)	6 / 59 (10.17%)
occurrences (all)	6	2	6
Injection site erythema			
subjects affected / exposed	0 / 54 (0.00%)	3 / 69 (4.35%)	2 / 59 (3.39%)
occurrences (all)	0	5	2
Malaise			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	2 / 59 (3.39%)
occurrences (all)	0	3	2
Injection site bruising			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	1 / 59 (1.69%)
occurrences (all)	0	2	1
Injection site rash			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	2 / 59 (3.39%)
occurrences (all)	0	1	2
Crying			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Feeling hot			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Thirst			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Chest discomfort			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Cyst			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Feeling abnormal			

subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Gait disturbance			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Injection site pruritus			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Local swelling			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Localised oedema			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Sluggishness			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Temperature intolerance			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Xerosis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Benign prostatic hyperplasia			

subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Genital hypoaesthesia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Haematospermia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Menstruation irregular			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Sexual dysfunction			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Testicular pain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 54 (7.41%)	5 / 69 (7.25%)	5 / 59 (8.47%)
occurrences (all)	4	5	5
Cough			
subjects affected / exposed	4 / 54 (7.41%)	6 / 69 (8.70%)	0 / 59 (0.00%)
occurrences (all)	4	6	0
Dyspnoea exertional			
subjects affected / exposed	0 / 54 (0.00%)	4 / 69 (5.80%)	2 / 59 (3.39%)
occurrences (all)	0	4	2
Epistaxis			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	2 / 59 (3.39%)
occurrences (all)	0	2	2
Oropharyngeal pain			
subjects affected / exposed	2 / 54 (3.70%)	2 / 69 (2.90%)	0 / 59 (0.00%)
occurrences (all)	2	2	0
Wheezing			

subjects affected / exposed	0 / 54 (0.00%)	3 / 69 (4.35%)	1 / 59 (1.69%)
occurrences (all)	0	3	1
Respiratory tract congestion			
subjects affected / exposed	1 / 54 (1.85%)	2 / 69 (2.90%)	0 / 59 (0.00%)
occurrences (all)	1	2	0
Rhinorrhoea			
subjects affected / exposed	2 / 54 (3.70%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	2	1	0
Nasal congestion			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Sneezing			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Dry throat			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hiccups			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Increased viscosity of nasal secretion			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal plaque			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Pharyngeal oedema			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Throat irritation			

subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Throat tightness			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	9 / 54 (16.67%)	14 / 69 (20.29%)	14 / 59 (23.73%)
occurrences (all)	9	15	16
Depression			
subjects affected / exposed	5 / 54 (9.26%)	7 / 69 (10.14%)	4 / 59 (6.78%)
occurrences (all)	6	8	4
Mood swings			
subjects affected / exposed	2 / 54 (3.70%)	5 / 69 (7.25%)	3 / 59 (5.08%)
occurrences (all)	2	5	3
Anxiety			
subjects affected / exposed	3 / 54 (5.56%)	3 / 69 (4.35%)	2 / 59 (3.39%)
occurrences (all)	3	3	2
Sleep disorder			
subjects affected / exposed	1 / 54 (1.85%)	2 / 69 (2.90%)	1 / 59 (1.69%)
occurrences (all)	1	2	1
Abnormal dreams			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	2 / 59 (3.39%)
occurrences (all)	0	0	3
Affect lability			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Anger			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Restlessness			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	1	1	0

Anxiety disorder			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Bipolar disorder			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Bruxism			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Depressed mood			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Hallucination			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Libido decreased			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Mood altered			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Panic disorder			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Stress			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Suicidal ideation			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Investigations			
Weight decreased			
subjects affected / exposed	3 / 54 (5.56%)	6 / 69 (8.70%)	1 / 59 (1.69%)
occurrences (all)	3	6	1
Neutrophil count decreased			

subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	3 / 59 (5.08%)
occurrences (all)	1	1	3
Blood uric acid increased			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	2 / 59 (3.39%)
occurrences (all)	1	1	3
CD4 lymphocytes decreased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	2 / 59 (3.39%)
occurrences (all)	0	1	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	1 / 59 (1.69%)
occurrences (all)	0	2	1
Blood bilirubin increased			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	2	0	2
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Blood creatine increased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	2
Blood lactate dehydrogenase increased			

subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Blood triglycerides increased			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Creatinine renal clearance decreased			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram abnormal			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Eosinophil count increased			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Haematocrit decreased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
International normalised ratio increased			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Liver function test abnormal			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1

Neutrophil count increased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Prothrombin time prolonged			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Reticulocyte count decreased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Weight increased			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	2
Contusion			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Excoriation			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Joint dislocation			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Joint injury			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Laceration			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Ligament sprain			

subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Transfusion reaction			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Colour blindness			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	4
Tachycardia			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Atrioventricular block first degree			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Bundle branch block left			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Mitral valve incompetence			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Myocardial ischaemia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Tricuspid valve incompetence			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Ventricular extrasystoles			

subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 54 (27.78%)	17 / 69 (24.64%)	20 / 59 (33.90%)
occurrences (all)	17	18	23
Dizziness			
subjects affected / exposed	6 / 54 (11.11%)	6 / 69 (8.70%)	6 / 59 (10.17%)
occurrences (all)	7	6	7
Dysgeusia			
subjects affected / exposed	2 / 54 (3.70%)	10 / 69 (14.49%)	5 / 59 (8.47%)
occurrences (all)	2	10	5
Disturbance in attention			
subjects affected / exposed	0 / 54 (0.00%)	4 / 69 (5.80%)	4 / 59 (6.78%)
occurrences (all)	0	4	4
Paraesthesia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	5 / 59 (8.47%)
occurrences (all)	1	0	5
Hypoaesthesia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	4 / 59 (6.78%)
occurrences (all)	0	0	5
Dizziness postural			
subjects affected / exposed	2 / 54 (3.70%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	2	0	1
Syncope			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	1 / 59 (1.69%)
occurrences (all)	0	5	1
Hypersomnia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Memory impairment			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Migraine			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	1	1	0

Neuropathy peripheral			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Somnolence			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Tremor			
subjects affected / exposed	2 / 54 (3.70%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Ageusia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Allodynia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Amnesia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Burning sensation			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Head discomfort			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Hyperaesthesia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Lethargy			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Parosmia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0

Presyncope			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Sensory disturbance			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	15 / 54 (27.78%)	21 / 69 (30.43%)	16 / 59 (27.12%)
occurrences (all)	17	23	20
Neutropenia			
subjects affected / exposed	10 / 54 (18.52%)	15 / 69 (21.74%)	4 / 59 (6.78%)
occurrences (all)	13	23	6
Thrombocytopenia			
subjects affected / exposed	1 / 54 (1.85%)	5 / 69 (7.25%)	0 / 59 (0.00%)
occurrences (all)	1	6	0
Lymphadenopathy			
subjects affected / exposed	1 / 54 (1.85%)	2 / 69 (2.90%)	0 / 59 (0.00%)
occurrences (all)	1	2	0
Pancytopenia			
subjects affected / exposed	3 / 54 (5.56%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	3	0	0
Haemolytic anaemia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Lymph node pain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Lymphoid tissue hyperplasia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			

subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Ear pruritus			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Hyperacusis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Photophobia			
subjects affected / exposed	2 / 54 (3.70%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	2	1	1
Vision blurred			
subjects affected / exposed	2 / 54 (3.70%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	2	1	1
Dry eye			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Ocular hyperaemia			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Visual impairment			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Abnormal sensation in eye			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Blepharitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis allergic			

subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Eye discharge			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Eye inflammation			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Eye pruritus			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Hypermetropia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Ocular icterus			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	23 / 54 (42.59%)	22 / 69 (31.88%)	19 / 59 (32.20%)
occurrences (all)	27	26	23
Diarrhoea			
subjects affected / exposed	13 / 54 (24.07%)	21 / 69 (30.43%)	6 / 59 (10.17%)
occurrences (all)	14	22	6
Vomiting			
subjects affected / exposed	10 / 54 (18.52%)	11 / 69 (15.94%)	11 / 59 (18.64%)
occurrences (all)	10	14	15
Anorectal discomfort			
subjects affected / exposed	6 / 54 (11.11%)	11 / 69 (15.94%)	9 / 59 (15.25%)
occurrences (all)	6	11	10
Anal pruritus			
subjects affected / exposed	4 / 54 (7.41%)	10 / 69 (14.49%)	6 / 59 (10.17%)
occurrences (all)	4	10	6

Haemorrhoids			
subjects affected / exposed	2 / 54 (3.70%)	11 / 69 (15.94%)	2 / 59 (3.39%)
occurrences (all)	2	11	3
Dry mouth			
subjects affected / exposed	4 / 54 (7.41%)	1 / 69 (1.45%)	5 / 59 (8.47%)
occurrences (all)	4	1	5
Constipation			
subjects affected / exposed	2 / 54 (3.70%)	5 / 69 (7.25%)	1 / 59 (1.69%)
occurrences (all)	2	5	1
Abdominal pain			
subjects affected / exposed	2 / 54 (3.70%)	4 / 69 (5.80%)	1 / 59 (1.69%)
occurrences (all)	2	4	1
Cheilitis			
subjects affected / exposed	1 / 54 (1.85%)	2 / 69 (2.90%)	3 / 59 (5.08%)
occurrences (all)	1	2	3
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 54 (3.70%)	2 / 69 (2.90%)	2 / 59 (3.39%)
occurrences (all)	2	2	2
Aphthous stomatitis			
subjects affected / exposed	2 / 54 (3.70%)	2 / 69 (2.90%)	1 / 59 (1.69%)
occurrences (all)	2	2	1
Dyspepsia			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	3 / 59 (5.08%)
occurrences (all)	0	2	3
Abdominal pain upper			
subjects affected / exposed	0 / 54 (0.00%)	4 / 69 (5.80%)	0 / 59 (0.00%)
occurrences (all)	0	4	0
Proctalgia			
subjects affected / exposed	0 / 54 (0.00%)	3 / 69 (4.35%)	1 / 59 (1.69%)
occurrences (all)	0	3	1
Rectal haemorrhage			
subjects affected / exposed	1 / 54 (1.85%)	3 / 69 (4.35%)	0 / 59 (0.00%)
occurrences (all)	1	3	0
Flatulence			
subjects affected / exposed	2 / 54 (3.70%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	2	1	0

Oral pain			
subjects affected / exposed	0 / 54 (0.00%)	3 / 69 (4.35%)	0 / 59 (0.00%)
occurrences (all)	0	4	0
Abdominal discomfort			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Anal ulcer			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Gastritis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	2	0	1
Gingival pain			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	0 / 59 (0.00%)
occurrences (all)	0	3	0
Glossodynia			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Haematochezia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Loose tooth			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Toothache			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Abdominal distension			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Abnormal faeces			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Anal fissure			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1

Anorectal disorder			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Chapped lips			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Dental caries			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Eructation			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Faeces discoloured			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Faeces hard			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Frequent bowel movements			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Gastrointestinal tract irritation			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Gingival bleeding			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Lip dry			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0

Odynophagia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Oesophageal pain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Oral discomfort			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Oral mucosal erythema			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Palatal disorder			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Rectal fissure			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Retching			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Sensitivity of teeth			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Tongue disorder			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Tongue eruption			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Jaundice			

subjects affected / exposed	3 / 54 (5.56%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	3	0	1
Cholelithiasis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	22 / 54 (40.74%)	21 / 69 (30.43%)	18 / 59 (30.51%)
occurrences (all)	25	22	20
Rash			
subjects affected / exposed	16 / 54 (29.63%)	20 / 69 (28.99%)	11 / 59 (18.64%)
occurrences (all)	23	25	15
Alopecia			
subjects affected / exposed	1 / 54 (1.85%)	4 / 69 (5.80%)	2 / 59 (3.39%)
occurrences (all)	1	4	2
Dry skin			
subjects affected / exposed	2 / 54 (3.70%)	3 / 69 (4.35%)	2 / 59 (3.39%)
occurrences (all)	2	3	2
Pruritus generalised			
subjects affected / exposed	2 / 54 (3.70%)	1 / 69 (1.45%)	4 / 59 (6.78%)
occurrences (all)	2	1	4
Rash pruritic			
subjects affected / exposed	2 / 54 (3.70%)	3 / 69 (4.35%)	2 / 59 (3.39%)
occurrences (all)	2	4	2
Eczema			
subjects affected / exposed	2 / 54 (3.70%)	2 / 69 (2.90%)	1 / 59 (1.69%)
occurrences (all)	2	2	2
Rash papular			
subjects affected / exposed	2 / 54 (3.70%)	2 / 69 (2.90%)	1 / 59 (1.69%)
occurrences (all)	2	2	1
Night sweats			
subjects affected / exposed	3 / 54 (5.56%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	3	1	0
Rash erythematous			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	2 / 59 (3.39%)
occurrences (all)	1	1	2

Rash maculo-papular			
subjects affected / exposed	2 / 54 (3.70%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	2	1	1
Erythema			
subjects affected / exposed	1 / 54 (1.85%)	2 / 69 (2.90%)	0 / 59 (0.00%)
occurrences (all)	1	2	0
Acne			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	2 / 59 (3.39%)
occurrences (all)	0	0	3
Dermatitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	2 / 59 (3.39%)
occurrences (all)	0	0	2
Macule			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Photosensitivity reaction			
subjects affected / exposed	2 / 54 (3.70%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Rash morbilliform			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	2 / 59 (3.39%)
occurrences (all)	0	0	2
Skin fissures			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	2 / 59 (3.39%)
occurrences (all)	0	0	2
Angioedema			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Cold sweat			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Dermatitis acneiform			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0

Dermatitis contact			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Dermatosis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Erythema multiforme			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Nail disorder			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Neurodermatitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Pigmentation disorder			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Psoriasis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Rash generalised			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Seborrhoea			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Skin disorder			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Skin exfoliation			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0

Skin hypopigmentation			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Skin mass			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Pyuria			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Enuresis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Nephropathy			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Nocturia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Polyuria			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Renal failure acute			

subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	2 / 54 (3.70%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	2	0	1
Hypogonadism			
subjects affected / exposed	2 / 54 (3.70%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	8 / 54 (14.81%)	9 / 69 (13.04%)	9 / 59 (15.25%)
occurrences (all)	8	9	9
Arthralgia			
subjects affected / exposed	5 / 54 (9.26%)	5 / 69 (7.25%)	3 / 59 (5.08%)
occurrences (all)	5	6	3
Back pain			
subjects affected / exposed	5 / 54 (9.26%)	3 / 69 (4.35%)	1 / 59 (1.69%)
occurrences (all)	6	3	1
Pain in extremity			
subjects affected / exposed	1 / 54 (1.85%)	2 / 69 (2.90%)	3 / 59 (5.08%)
occurrences (all)	1	3	3
Bone pain			
subjects affected / exposed	2 / 54 (3.70%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	2	2	1
Muscle spasms			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	1	1	1
Neck pain			
subjects affected / exposed	2 / 54 (3.70%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	2	2	0
Flank pain			

subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Joint stiffness			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Joint swelling			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Muscle haemorrhage			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Osteopenia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Osteoporosis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Pain in jaw			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Rhabdomyolysis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Spinal osteoarthritis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	5 / 59 (8.47%)
occurrences (all)	1	1	7

Folliculitis			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	2 / 59 (3.39%)
occurrences (all)	1	1	2
Influenza			
subjects affected / exposed	3 / 54 (5.56%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	3	1	0
Sinusitis			
subjects affected / exposed	1 / 54 (1.85%)	2 / 69 (2.90%)	1 / 59 (1.69%)
occurrences (all)	2	2	1
Bronchitis			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	1	1	1
Oral candidiasis			
subjects affected / exposed	2 / 54 (3.70%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	2	0	1
Pharyngitis			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	1 / 59 (1.69%)
occurrences (all)	0	2	2
Tooth infection			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	2 / 59 (3.39%)
occurrences (all)	0	1	2
Urinary tract infection			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	1	1	2
Cellulitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Hordeolum			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Nasopharyngitis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	2 / 59 (3.39%)
occurrences (all)	0	0	2
Onychomycosis			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	1	1	0

Otitis media			
subjects affected / exposed	2 / 54 (3.70%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Pneumonia			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Abscess jaw			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Abscess limb			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Abscess soft tissue			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Body tinea			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Cardiac valve vegetation			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Eye infection			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Furuncle			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis viral			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0

Gingivitis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Injection site pustule			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Mycoplasma infection			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Otitis externa			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Sepsis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Staphylococcal skin infection			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Tinea cruris			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Urethritis chlamydial			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1

Urethritis gonococcal			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 54 (14.81%)	11 / 69 (15.94%)	8 / 59 (13.56%)
occurrences (all)	9	12	8
Hypokalaemia			
subjects affected / exposed	1 / 54 (1.85%)	6 / 69 (8.70%)	4 / 59 (6.78%)
occurrences (all)	1	6	4
Dehydration			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	2 / 59 (3.39%)
occurrences (all)	0	4	2
Diabetes mellitus			
subjects affected / exposed	0 / 54 (0.00%)	2 / 69 (2.90%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Hypophosphataemia			
subjects affected / exposed	1 / 54 (1.85%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	1	1	0
Abnormal loss of weight			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Acidosis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Gout			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hyperamylasaemia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hyperlipasaemia			

subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hyperuricaemia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 69 (1.45%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 69 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 69 (0.00%)	0 / 59 (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
09 September 2011	Made several changes to the schedule of assessments. Revised inclusion and exclusion criteria. Included specification that one of the IDMC reviews will occur when 10 prior null responder subjects receiving non-EFV HAART regimen reached Week 4. Included RAL in predefined HAART medications for PK evaluations. Included dose modifications based on CD4 counts and HIV RNA results.
22 December 2011	Modified timing of serial PK samples. Provided further detail regarding undetectable HCV RNA results (LLOQ and LOD). Modified exclusion for participation in any concurrent research study- observational studies that include blood draws are permitted. Included instruction regarding repeat testing and confirmation of HCV RNA results. Included clarification reference to DAIDS for grading the intensity of certain clinical events and laboratory abnormalities. Included reference to Investigator's Brochure for prohibited antihistamines.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

It was decided by Sponsor on 13 January 2014 to terminate the study early at the primary efficacy endpoint (SVR12) as part of a decision to modify the drug development plan. Eligible subjects completed virologic follow-up after termination.

Notes: