Clinical trial results:
A Phase IIb Study Evaluating a Long-Acting Intramuscular Regimen of GSK1265744 plus TMC278 For The Maintenance of Virologic Suppression Following an Induction of Virologic Suppression on an Oral regimen of GSK1265744 plus Abacavir/Lamivudine in HIV-1 Infected, Antiretroviral Therapy-Naive Adult Subjects

Summary

EudraCT number	2013-000783-29
Trial protocol	DE ES
Global end of trial date	

Results information

Result version number	v1
This version publication date	23 April 2016
First version publication date	23 April 2016

Trial information

Trial identification

Sponsor protocol code	200056

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	Interim
Date of interim/final analysis	13 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 December 2015
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To select an intramuscular dosing regimen of GSK744 LA plus TMC278 LA based on a comparison of the Week 32 antiviral activity, tolerability, and safety of two IM dosing regimens, relative to GSK744 30 mg plus Abacavir/Lamivudine (ABC/3TC) orally once daily.

Protection of trial subjects:

An IDMC committee will evaluate the efficacy, tolerability, and safety of cabotegravir (CAB) and Rilpivirine (RPV) at the following times: before all eligible subjects have transitioned from the Induction Period to the Maintenance Period; after approximately 45 subjects have reached Week 8 of the Maintenance Period. Futility guidance (e.g., a Bayesian posterior probability approach when 50% of subjects have completed Week 24 of the Maintenance Period) is included to monitor the performance of all treatment arms in order to prevent subjects from continuing on a dosing regimen if existing data indicates that subjects are at unacceptable risk of inadequate maintenance of virologic suppression.

A CAB treatment arm should be recommended to stop if there is an indication of any safety signal/effect that would not support continuation of one or more of the CAB treatment groups. This should take into consideration any of the following which are felt to be clinically significant:
I. Serious adverse events (e.g. liver event).
II. Combinations of non-serious events.
III. Treatment-limiting adverse events.
IV. Unacceptable number of protocol defined virologic failures with CAB or RPV resistance defined as at least 3 or more virologic failures comprising of ≥ 20% of the treated subjects in an IM treatment arm.
V. Mean predose concentrations for the long acting (LA) treatment arm less than 1x protein-adjusted 90% inhibitory concentration (PAIC) 90 (0.166 µg/mL) for CAB and less than 12ng/mL for RPV.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 April 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Ethical reason, Regulatory reason, Scientific research
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 34
Country: Number of subjects enrolled	United States: 84
Country: Number of subjects enrolled	Spain: 104
Country: Number of subjects enrolled	France: 36
Country: Number of subjects enrolled	Germany: 52
Worldwide total number of subjects	310
EEA total number of subjects	192

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)	310
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Cabotegravir (CAB) is the oral formulation (OF) of GSK1265744, CAB LA is the long acting (LA) injectable formulation of GSK1265744, Rilpivirine (RPV) is the OF of RPV, and RPV LA is the LA injectable formulation of RPV.

Pre-assignment

Screening details:

Study consisted of 28 days Screening Period, 20 weeks Induction Period (IP), 96 weeks Maintenance Period (MP), Extension Period (EP) and 52 weeks Long-Term Follow Up Period (LTFP). A total of 310 participants (par.) enrolled, 309 received >1 dose investigational product, and 288 completed IP, of which 286 were qualified and randomized into the MP.

Period 1

Period 1 title	Induction Period (20 Weeks)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	CAB 30 mg + ABC/3TC once daily

Arm description:

Participants received a combination of an oral regimen of CAB 30 milligrams (mg) once daily plus Abacavir/Lamivudine (ABC/3TC) 600/300 mg once daily for 20 weeks and also received an oral formulation of RPV 25 mg tablet once daily in the last 4 weeks of the IP.

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

Dosage and administration details:

Cabotegravir (CAB) Oral Tablet was formulated as white to almost white oval shaped film coated 30 mg tablets for oral administration. In IP, participants received CAB 30 mg once daily for 20 weeks

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

Dosage and administration details:

Abacavir/Lamivudine (ABC/3TC)was supplied as fixed dose combination (FDC) oral tablet, which contained 600 mg of ABC (as abacavir sulfate) and 300 mg of 3TC. The tablets were orange, film-coated, modified capsule-shaped and debossed with "GS FC2" on one side with no markings on the reverse side. ABC/3TC was packaged in bottles of 30 tablets. In IP, participants received ABC/3TC 600/300 mg once daily for 20 weeks.

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

Dosage and administration details:

Rilpivirine (RPV) Oral Tablet was supplied as a 25 mg tablet that was off-white, round, biconvex, film-coated and debossed on one side with “TMC” and the other side with “25”. Participants received RPV 25 mg tablet once daily in last 4 weeks of IP.

Number of subjects in period 1[1]	CAB 30 mg + ABC/3TC once daily
Started	309
Completed	288
Not completed	21
Adverse event, serious fatal	1
Physician decision	1
Consent withdrawn by subject	5
Adverse event, non-fatal	2
Lost to follow-up	2
Lack of efficacy	5
Protocol deviation	2
Protocol-Defined Stopping Criteria	3

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Study consisted of 28 days Screening Period, 20 weeks Induction Period (IP), 96 weeks Maintenance Period (MP), Extension Period (EP) and 52 weeks Long-Term Follow Up Period (LTFP). A total of 310 participants (par.) enrolled, 309 received >1 dose investigational product, and 288 completed IP, of which 286 were qualified and randomized into the MP.

Period 2

Period 2 title	Maintenance Period (96 weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	CAB LA 600 mg + RPV LA 900 mg IM - Q8W

Arm description:

In the IP of 20 weeks, participants received an oral regimen of CAB 30 mg once daily plus ABC/3TC 600/300 mg once daily. In the last 4 weeks of the IP, participants also received RPV 25 mg tablet once daily. In the MP, participants who were randomized to this arm received following intra muscular (IM) doses: Day 1 only – CAB LA 800 mg (loading dose delivered as two 400 mg IM injections) + RPV LA 900 mg IM. Week 4 only - CAB LA 600 mg IM (second loading dose, no RPV). Week 8 - CAB LA 600 mg IM + RPV LA 900 mg IM every 8 Weeks (Q8W) for 96 weeks

Arm type	Experimental

Investigational medicinal product name	Cabotegravir Injectable Suspension
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

CAB Injectable Suspension was a sterile white to slightly colored suspension containing 200 mg/mL of CAB as free acid for administration by intramuscular (IM) injection. The product was packaged in a 3 mL United States Pharmacopeia (USP) Type I glass vial with a 13 mm gray stopper and aluminium seal. Each vial was for single use containing a withdrawable volume of 2.0 mL, and did not require dilution prior to administration. Participants randomized to Q8W regimen arm received following intra muscular (IM) doses: Day 1 only – CAB LA 800 mg (loading dose delivered as two 400 mg IM injections). Week 4 only - CAB LA 600 mg IM. Week 8 - CAB LA 600 mg IM every 8 Weeks (Q8W) for 96 weeks.

Investigational medicinal product name	Rilpivirine Injectable Suspension
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Rilpivirine Injectable Suspension was a sterile white suspension containing 300 mg/mL of TMC278 as free base for administration by intramuscular (IM) injection. The product was packaged in a 2 mL USP Type I glass vial with a 13 mm grey stopper and aluminium seal. Each vial was for single use containing a nominal fill of 2.0 mL, and did not require dilution prior to administration but required refrigeration. Participants randomized to Q8W regimen arm received following intra muscular (IM) doses: RPV LA 900 mg IM every 8 Weeks (Q8W) for 96 weeks

Arm title	CAB LA 400 mg + RPV LA 600 mg IM - Q4W

Arm description:

In the IP of 20 weeks, participants received an oral regimen of CAB 30 mg once daily plus ABC/3TC 600/300 mg once daily. In the last 4 weeks of the IP, participants also received RPV 25 mg tablet once daily. In the MP, participants who were randomized to this arm received following IM doses: Day 1 only - CAB LA 800 mg (loading dose delivered as two 400 mg IM injections) + RPV LA 600 mg IM. Week 4 - CAB LA 400 mg IM + RPV LA 600 mg IM every 4 weeks (Q4W) for 96 weeks.

Arm type	Experimental
Investigational medicinal product name	Cabotegravir Injectable Suspension
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

CAB Injectable Suspension was a sterile white to slightly colored suspension containing 200 mg/mL of CAB as free acid for administration by intramuscular (IM) injection. The product was packaged in a 3 mL USP Type I glass vial with a 13 mm gray stopper and aluminium seal. Each vial was for single use containing a withdrawable volume of 2.0 mL, and did not require dilution prior to administration. Participants randomized to Q4W regimen arm received following IM doses: Day 1 only - CAB LA 800 mg (loading dose delivered as two 400 mg IM injections). Week 4 - CAB LA 400 mg IM + every 4 weeks (Q4W) for 96 weeks

Investigational medicinal product name	Rilpivirine Injectable Suspension
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Rilpivirine Injectable Suspension was a sterile white suspension containing 300 mg/mL of TMC278 as free base for administration by intramuscular (IM) injection. The product was packaged in a 2 mL USP Type I glass vial with a 13 mm grey stopper and aluminium seal. Each vial was for single use containing a nominal fill of 2.0 mL, and did not require dilution prior to administration but required refrigeration. Participants randomized to Q4W regimen arm received following IM doses: RPV LA 600 mg IM every 4

weeks (Q4W) for 96 weeks.

Arm title	CAB 30 mg + ABC/3TC once daily orally

Arm description:

In the IP of 20 weeks, participants received an oral regimen of CAB 30 mg once daily plus ABC/3TC 600/300 mg once daily. In the last 4 weeks of the IP, participants also received RPV 25 mg tablet once daily. In the MP, participants who were randomized to this arm received an oral regimen of 30 mg of CAB and ABC/3TC once daily for 96 weeks (or 104 weeks if going on to the EP).

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

Dosage and administration details:

Cabotegravir (CAB) Oral Tablet was formulated as white to almost white oval shaped film coated 30 mg tablets for oral administration. In the MP, participants randomized in oral regimen arm (CAB 30 mg + ABC/3TC) received 30 mg of CAB once daily for 96 weeks (or 104 weeks if going on to the EP).

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

Dosage and administration details:

Abacavir/Lamivudine (ABC/3TC)was supplied as fixed dose combination (FDC) oral tablet, which contained 600 mg of ABC (as abacavir sulfate) and 300 mg of 3TC. The tablets were orange, film-coated, modified capsule-shaped and debossed with GS FC2 on one side with no markings on the reverse side. ABC/3TC was packaged in bottles of 30 tablets. In the MP, participants randomized in oral regimen arm (CAB 30 mg + ABC/3TC) received ABC/3TC 600/300 mg once daily for 96 weeks (or 104 weeks if going on to the EP).

Number of subjects in period 2[2]	CAB LA 600 mg + RPV LA 900 mg IM - Q8W	CAB LA 400 mg + RPV LA 600 mg IM - Q4W	CAB 30 mg + ABC/3TC once daily orally
Started	115	115	56
Completed	0	0	0
Not completed	115	115	56
Adverse event, serious fatal	-	1	-
Withdrew Consent	-	-	1
Ongoing at time of analysis	112	105	50
Adverse event, non-fatal	-	5	1
Subject Relocated	-	1	1
Intolerability of Injections	2	-	-
Lost to follow-up	-	-	1
Lack of efficacy	1	-	1

Protocol deviation	-	2	-
Protocol-Defined Stopping Criteria	-	1	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Study consisted of 28 days Screening Period, 20 weeks Induction Period (IP), 96 weeks Maintenance Period (MP), Extension Period (EP) and 52 weeks Long-Term Follow Up Period (LTFP). A total of 310 participants (par.) enrolled, 309 received >1 dose investigational product, and 288 completed IP, of which 286 were qualified and randomized into the MP.

Baseline characteristics

Reporting groups	
Reporting group title	CAB 30 mg + ABC/3TC once daily
Reporting group description:	
Participants received a combination of an oral regimen of CAB 30 milligrams (mg) once daily plus Abacavir/Lamivudine (ABC/3TC) 600/300 mg once daily for 20 weeks and also received an oral formulation of RPV 25 mg tablet once daily in the last 4 weeks of the IP.	

Reporting group values	CAB 30 mg + ABC/3TC once daily	Total	
Number of subjects	309	309	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	36.6		
standard deviation	± 10.39	-	
Gender categorical			
Units: Subjects			
Female	27	27	
Male	282	282	
Race, Customized			
Units: Subjects			
African American/African Heritage	46	46	
American Indian or Alaskan Native	10	10	
Asian - Central/South Asian Heritage	1	1	
Asian - Japanese Heritage	1	1	
Asian - South East Asian Heritage	2	2	
Native Hawaiian or Other Pacific Islander	1	1	
White - Arabic/North African Heritage	6	6	
White - White/Caucasian/European Heritage	240	240	
Mixed Race	2	2	

End points

End points reporting groups

Reporting group title	CAB 30 mg + ABC/3TC once daily

Reporting group description:

Participants received a combination of an oral regimen of CAB 30 milligrams (mg) once daily plus Abacavir/Lamivudine (ABC/3TC) 600/300 mg once daily for 20 weeks and also received an oral formulation of RPV 25 mg tablet once daily in the last 4 weeks of the IP.

Reporting group title	CAB LA 600 mg + RPV LA 900 mg IM - Q8W

Reporting group description:

In the IP of 20 weeks, participants received an oral regimen of CAB 30 mg once daily plus ABC/3TC 600/300 mg once daily. In the last 4 weeks of the IP, participants also received RPV 25 mg tablet once daily. In the MP, participants who were randomized to this arm received following intra muscular (IM) doses: Day 1 only – CAB LA 800 mg (loading dose delivered as two 400 mg IM injections) + RPV LA 900 mg IM. Week 4 only - CAB LA 600 mg IM (second loading dose, no RPV). Week 8 - CAB LA 600 mg IM + RPV LA 900 mg IM every 8 Weeks (Q8W) for 96 weeks

Reporting group title	CAB LA 400 mg + RPV LA 600 mg IM - Q4W

Reporting group description:

In the IP of 20 weeks, participants received an oral regimen of CAB 30 mg once daily plus ABC/3TC 600/300 mg once daily. In the last 4 weeks of the IP, participants also received RPV 25 mg tablet once daily. In the MP, participants who were randomized to this arm received following IM doses: Day 1 only - CAB LA 800 mg (loading dose delivered as two 400 mg IM injections) + RPV LA 600 mg IM. Week 4 - CAB LA 400 mg IM + RPV LA 600 mg IM every 4 weeks (Q4W) for 96 weeks.

Reporting group title	CAB 30 mg + ABC/3TC once daily orally

Reporting group description:

In the IP of 20 weeks, participants received an oral regimen of CAB 30 mg once daily plus ABC/3TC 600/300 mg once daily. In the last 4 weeks of the IP, participants also received RPV 25 mg tablet once daily. In the MP, participants who were randomized to this arm received an oral regimen of 30 mg of CAB and ABC/3TC once daily for 96 weeks (or 104 weeks if going on to the EP).

Primary: Percentage of participants with plasma Human Immunodeficiency Virus-1 (HIV-1) Ribonucleic Acid (RNA) level below 50 copies/milliliter (c/mL) at Week 32 based on the using the Missing, Switch, or Discontinuation = Failure (MSDF) algorithm

End point title	Percentage of participants with plasma Human Immunodeficiency Virus-1 (HIV-1) Ribonucleic Acid (RNA) level below 50 copies/milliliter (c/mL) at Week 32 based on the using the Missing, Switch, or Discontinuation = Failure (MSDF) algorithm

End point description:

Percentage of par. with Plasma HIV-1 RNA <50 c/mL at Week (Wk) 32 was assessed using the MSDF, as codified by the FDA "snapshot" algorithm. This algorithm treated all par. without HIV-1 RNA data at Wk 32 as nonresponders, as well as par. who switched their concomitant antiretroviral therapy (ART) prior to Wk 32 as follows: background ART substitutions non-permitted per protocol; background ART substitutions permitted per protocol but prescribed while not suppressed, 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 par. was on-treatment within the Wk 32 time window: +/- 2-Wk window, followed by +/- 6-Wk window only if necessary to obtain data in window. ITT-ME Population consisted of all randomized par. who received at least one dose of investigational product during the MP of the study.

End point type	Primary

End point timeframe:

Week 32

End point values	CAB LA 600 mg + RPV LA 900 mg IM - Q8W	CAB LA 400 mg + RPV LA 600 mg IM - Q4W	CAB 30 mg + ABC/3TC once daily orally	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	115[1]	115[2]	56[3]	
Units: Percentage of participants				
number (not applicable)	95	94	91	

Notes:

[1] - Intent-To-Treat Exposed (ITT-ME) Population

[2] - Intent-To-Treat Exposed (ITT-ME) Population

[3] - Intent-To-Treat Exposed (ITT-ME) Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	CAB LA 600 mg + RPV LA 900 mg IM - Q8W v CAB 30 mg + ABC/3TC once daily orally
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentage
Point estimate	3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	12.2

Statistical analysis title	Statistical analysis 2
Comparison groups	CAB LA 400 mg + RPV LA 600 mg IM - Q4W v CAB 30 mg + ABC/3TC once daily orally
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percentage
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	11.5

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Posterior probability that the true difference in response rates (Q8W – Oral CAB) is greater than -10% was calculated according to a Bayesian model assuming Beta(23,2) and Beta(1,1) prior distributions for the Q8W and Oral CAB response rates, respectively. A posterior probability of at least 90% corresponds to substantial evidence of positive outcome and is pre specified as the weight of evidence threshold for concluding that the IM dosing regimen (Q8W) is comparable to the Oral CAB regimen.

Comparison groups	CAB LA 600 mg + RPV LA 900 mg IM - Q8W v CAB 30 mg + ABC/3TC once daily orally
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	other
P-value	= 100 [4]
Method	Bayesian posterior probability percent

Notes:

[4] - p-value field contains the Bayesian posterior probability percent

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Posterior probability that the true difference in response rates (Q4W – Oral CAB) is greater than -10% was calculated according to a Bayesian model assuming Beta(23,2) and Beta(1,1) prior distributions for the Q4W and Oral CAB response rates, respectively. A posterior probability of at least 90% corresponds to substantial evidence of positive outcome and is pre specified as the weight of evidence threshold for concluding that the IM dosing regimen (Q4W) is comparable to the Oral CAB regimen.

Comparison groups	CAB LA 400 mg + RPV LA 600 mg IM - Q4W v CAB 30 mg + ABC/3TC once daily orally
Number of subjects included in analysis	171
Analysis specification	Pre-specified
Analysis type	other
P-value	= 99.9 [5]
Method	Bayesian posterior probability percent

Notes:

[5] - p-value field contains the Bayesian posterior probability percent

Primary: Number of participants with protocol defined virologic failure (PDVF) during the Maintenance Period

End point title	Number of participants with protocol defined virologic failure (PDVF) during the Maintenance Period[6]

End point description:

Virologic failure is defined as any of the following: Non-response as indicated by a less than a 1.0 log10 copies/milliliter (c/mL) decrease in plasma HIV-1 RNA after 4 weeks of starting the IP (subsequently confirmed, unless the plasma HIV-1 RNA is <400 c/mL). Rebound as indicated by two consecutive plasma HIV-1 RNA levels >=200 c/mL after prior suppression to < 200 c/mL. Rebound as indicated by two consecutive plasma HIV-1 RNA that are > 0.5 log10 c/mL increase in plasma HIV-1 RNA from the nadir value on study, where the lowest HIV-1 RNA value is >=200 c/mL.

End point type	Primary

End point timeframe:

From the start of study treatment in the Maintenance Period up to Week 32

Notes:

[6] - 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: Statistical Analysis is not applicable for this Outcome Measure.

End point values	CAB LA 600 mg + RPV LA 900 mg IM - Q8W	CAB LA 400 mg + RPV LA 600 mg IM - Q4W	CAB 30 mg + ABC/3TC once daily orally	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	115[7]	115[8]	56[9]	
Units: Participants				
number (not applicable)	1	0	1	

Notes:

[7] - ITT-ME Population

[8] - ITT-ME Population

[9] - ITT-ME Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with all post-Baseline any adverse event (AE) or any serious adverse event (SAE)

End point title	Number of participants with all post-Baseline any adverse event (AE) or any serious adverse event (SAE)[10]

End point description:

An AE is defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. A SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or is a congenital anomaly/birth defect, important medical events which may require medical or surgical intervention, drug-induced liver injury with hyperbilirubinaemia. This includes all post-baseline IP and MP AEs,as well as LTFP AEs for participants not entering the extension period that occur within 35/63 days of last IM injection (Q4W/Q8W) up to and including the start date of LTFP antiretroviral therapy. Safety Maintenance Population consisted of all participants who entered the MP and received at least one dose of investigational product.

End point type	Primary

End point timeframe:

From the start of the investigational product up to an average of 59 weeks

Notes:

[10] - 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: Statistical Analysis is not applicable for this Outcome Measure.

End point values	CAB LA 600 mg + RPV LA 900 mg IM - Q8W	CAB LA 400 mg + RPV LA 600 mg IM - Q4W	CAB 30 mg + ABC/3TC once daily orally	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	115[11]	115[12]	56[13]	
Units: Participants				
number (not applicable)				
Any AE	115	113	52	
Any SAE	9	8	5	

Notes:

[11] - Safety Maintenance

[12] - Safety Maintenance

[13] - Safety Maintenance

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with post-Baseline adverse events by maximum toxicity Grade

End point title	Number of participants with post-Baseline adverse events by maximum toxicity Grade[14]

End point description:

An AE is defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. This includes all post-baseline IP and MP AEs,as well as LTFP AEs for participants not entering the extension period that occur within 35/63 days of last MP IM injection (Q4W/Q8W) up to and including the start date of LTFP antiretroviral therapy. Adverse events that occurred during the study were evaluated by the Investigator and graded according to the 2004 version of the Division of AIDS (DAIDS) grading criteria, where Grade 1-mild, Grade 2-moderate, Grade 3-severe, Grade 4-potentially life-threatening.

End point type	Primary

End point timeframe:

From the start of the investigational product up to an average of 59 weeks

Notes:

[14] - 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: Statistical Analysis is not applicable for this Outcome Measure.

End point values	CAB LA 600 mg + RPV LA 900 mg IM - Q8W	CAB LA 400 mg + RPV LA 600 mg IM - Q4W	CAB 30 mg + ABC/3TC once daily orally	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	115[15]	115[16]	56[17]	
Units: Participants				
number (not applicable)				
Any AE with maximum toxicity Grade 1	31	25	19	
Any AE with maximum toxicity Grade 2	67	72	29	
Any AE with maximum toxicity Grade 3	15	14	3	
Any AE with maximum toxicity Grade 4	2	2	1	

Notes:

[15] - Safety Maintenance

[16] - Safety Maintenance

[17] - Safety Maintenance

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with maximum post-Baseline emergent toxicities for clinical chemistry parameters

End point title	Number of participants with maximum post-Baseline emergent toxicities for clinical chemistry parameters[18]

End point description:

Clinical chemistry parameters aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), carbon dioxide(CO2) content/bicarbonate (HCO3), cholesterol, creatine kinase (CK), glucose, low density lipoprotein (LDL) cholesterol, lipase, potassium, and sodium, total bilirubin (TBIL) and triglycerides were evaluated throughout the study. Toxicity was assessed for all laboratory parameters and was automatically graded by the central lab according to the 2004 version of the DAIDS grading criteria, where Grade 1-mild, Grade 2-moderate, Grade 3-severe, Grade 4-potentially life-threatening. This includes all post-baseline treatment emergent IP and MP toxicities, as well as LTFP toxicities for participants not entering the extension period that occur within 35/63 days of last IM injection (Q4W/Q8W) up to and including the start date of LTFP antiretroviral therapy.

End point type	Primary

End point timeframe:

From the start of the investigational product up to an average of 59 weeks

Notes:

[18] - 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: Statistical Analysis is not applicable for this Outcome Measure.

End point values	CAB LA 600 mg + RPV LA 900 mg IM - Q8W	CAB LA 400 mg + RPV LA 600 mg IM - Q4W	CAB 30 mg + ABC/3TC once daily orally	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	115[19]	115[20]	56[21]	
Units: Participants				
number (not applicable)				
ALT, Grade 1	18	14	5	
ALT, Grade 2	2	4	1	
ALT, Grade 3	0	1	2	
ALT, Grade 4	2	2	0	
ALP, Grade 1	1	3	1	
ALP, Grade 2	0	0	0	
ALP, Grade 3	0	0	0	
ALP, Grade 4	0	0	0	
AST, Grade 1	17	14	7	
AST, Grade 2	6	6	1	
AST, Grade 3	1	5	2	
AST, Grade 4	2	1	0	
CO2/HCO3, Grade 1	44	53	16	
CO2/HCO3, Grade 2	5	3	2	
CO2/HCO3, Grade 3	0	0	0	
CO2/HCO3, Grade 4	0	0	0	
Cholesterol, Grade 1	27	33	12	
Cholesterol, Grade 2	8	14	4	
Cholesterol, Grade 3	0	1	1	
Cholesterol, Grade 4	0	0	0	
CK, Grade 1	12	14	9	
CK, Grade 2	5	5	2	
CK, Grade 3	4	6	4	
CK, Grade 4	6	5	0	
Creatinine, Grade 1	2	3	0	
Creatinine, Grade 2	2	0	0	
Creatinine, Grade 3	0	0	0	
Creatinine, Grade 4	0	0	0	
Glucose, Grade 1	25	26	10	
Glucose, Grade 2	12	12	4	
Glucose, Grade 3	1	1	0	
Glucose, Grade 4	0	0	0	
LDL, Grade 1	17	18	9	
LDL, Grade 2	8	4	4	
LDL, Grade 3	1	4	2	
LDL, Grade 4	0	0	0	
Lipase, Grade 1	9	9	7	
Lipase, Grade 2	13	9	3	
Lipase, Grade 3	7	1	2	
Lipase, Grade 4	2	0	1	
Potassium, Grade 1	4	4	1	
Potassium, Grade 2	0	0	0	
Potassium, Grade 3	0	0	0	
Potassium, Grade 4	0	0	1	
Sodium, Grade 1	16	17	8	

Sodium, Grade 2	0	1	0	
Sodium, Grade 3	0	0	0	
Sodium, Grade 4	0	0	0	
TBIL, Grade 1	12	8	3	
TBIL, Grade 2	4	4	0	
TBIL, Grade 3	0	1	0	
TBIL, Grade 4	0	0	0	
Triglycerides, Grade 1	0	0	0	
Triglycerides, Grade 2	0	4	1	
Triglycerides, Grade 3	1	2	0	
Triglycerides, Grade 4	0	0	0	

Notes:

[19] - Safety Maintenance

[20] - Safety Maintenance

[21] - Safety Maintenance

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with maximum post-Baseline emergent toxicities for clinical hematological parameters

End point title	Number of participants with maximum post-Baseline emergent toxicities for clinical hematological parameters[22]

End point description:

Clinical chemistry parameters, hemoglobin, platelet count, total neutrophils (total ANC – total absolute neutrophil) and white blood cell count were evaluated throughout the study. Toxicity was assessed for all laboratory parameters and was automatically graded by the central lab according to the 2004 version of the DAIDS grading criteria, where Grade 1-mild, Grade 2-moderate, Grade 3-severe, Grade 4-potentially life-threatening. This includes all post-baseline treatment emergent IP and MP toxicities, as well as LTFP toxicities for participants not entering the extension period that occur within 35/63 days of last IM injection (Q4W/Q8W) up to and including the start date of LTFP antiretroviral therapy.

End point type	Primary

End point timeframe:

From the start of the investigational product up to an average of 59 weeks

Notes:

[22] - 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: Statistical Analysis is not applicable for this Outcome Measure.

End point values	CAB LA 600 mg + RPV LA 900 mg IM - Q8W	CAB LA 400 mg + RPV LA 600 mg IM - Q4W	CAB 30 mg + ABC/3TC once daily orally	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	115[23]	115[24]	56[25]	
Units: Participants				
number (not applicable)				
Hemoglobin, Grade 1	3	1	3	
Hemoglobin, Grade 2	0	0	0	
Hemoglobin, Grade 3	0	0	0	
Hemoglobin, Grade 4	0	0	0	
Platelet count, Grade 1	3	4	0	
Platelet count, Grade 2	1	1	0	
Platelet count, Grade 3	0	0	0	
Platelet count, Grade 4	0	0	0	

Total Neutrophils, Grade 1	16	9	5	
Total Neutrophils, Grade 2	1	3	2	
Total Neutrophils, Grade 3	0	0	2	
Total Neutrophils, Grade 4	0	3	0	
White blood cell count, Grade 1	3	3	0	
White blood cell count, Grade 2	0	0	0	
White blood cell count, Grade 3	0	0	0	
White blood cell count, Grade 4	0	0	0	

Notes:

[23] - Safety Maintenance

[24] - Safety Maintenance

[25] - Safety Maintenance

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with maximum post-Baseline emergent urinalysis dipstick results

End point title	Number of participants with maximum post-Baseline emergent urinalysis dipstick results[26]

End point description:

Urinalysis dipstick included urine occult blood, urine glucose, urine ketones, urine nitrite, urine protein and urine leukocyte esterase test for detecting white blood cells. Dipstick results were categorized as: Traces, 1+, 2+, 3+ or Positive. Only those participants available at the specified time points were analyzed (represented by n=X, X, X in the category titles).

End point type	Primary

End point timeframe:

From the start of the investigational product up to an average of 59 weeks

Notes:

[26] - 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: Statistical Analysis is not applicable for this Outcome Measure.

End point values	CAB LA 600 mg + RPV LA 900 mg IM - Q8W	CAB LA 400 mg + RPV LA 600 mg IM - Q4W	CAB 30 mg + ABC/3TC once daily orally	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	115[27]	115[28]	56[29]	
Units: Participants				
number (not applicable)				
Urine Occult Blood Trace, n=10, 11, 4	5	6	1	
Urine Occult Blood 1+, n=10, 11, 4	3	3	2	
Urine Occult Blood 2+, n=10, 11, 4	0	0	0	
Urine Occult Blood 3+, n=10, 11, 4	2	2	1	
Urine Occult Blood Positive, n=10, 11, 4	0	0	0	
Urine Glucose Trace, n=1, 1, 1	1	0	0	
Urine Glucose 1+, n=1, 1, 1	0	0	1	
Urine Glucose 2+, n=1, 1, 1	0	1	0	
Urine Glucose 3+, n=1, 1, 1	0	0	0	
Urine Glucose Positive, n=1, 1, 1	0	0	0	
Urine Ketones Trace, n=16, 20, 10	12	17	8	
Urine Ketones 1+, n=16, 20, 10	4	3	2	
Urine Ketones 2+, n=16, 20, 10	0	0	0	

Urine Ketones 3+, n=16, 20, 10	0	0	0	
Urine Ketones Positive, n=16, 20, 10	0	0	0	
Urine Nitrite Trace, n=1, 3, 1	0	0	0	
Urine Nitrite 1+, n=1, 3, 1	0	0	0	
Urine Nitrite 2+, n=1, 3, 1	0	0	0	
Urine Nitrite 3+, n=1, 3, 1	0	0	0	
Urine Nitrite Positive, n=1, 3, 1	1	3	1	
Urine Protein Trace, n=17, 17, 7	15	11	2	
Urine Protein 1+, n=17, 17, 7	2	4	5	
Urine Protein 2+, n=17, 17, 7	0	2	0	
Urine Protein 3+, n=17, 17, 7	0	0	0	
Urine Protein Positive, n=17, 17, 7	0	0	0	
Urine Leukocyte Trace, n=20, 20, 8	8	10	3	
Urine Leukocyte 1+, n=20, 20, 8	7	8	3	
Urine Leukocyte 2+, n=20, 20, 8	4	0	1	
Urine Leukocyte 3+, n=20, 20, 8	1	2	1	
Urine Leukocyte Positive, n=20, 20, 8	0	0	0	

Notes:

[27] - Safety Maintenance

[28] - Safety Maintenance

[29] - Safety Maintenance

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Post-baseline serious adverse events (SAEs) and non-serious adverse events (AEs), defined as those events collected from the start of study treatment and until the follow up contact (up to an average of 59 weeks).

Adverse event reporting additional description:

SAEs and non-serious AEs were reported for members of the Safety Maintenance population consisted of all participants who entered the MP and received at least one dose of investigational product.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	CAB LA 600 mg + RPV LA 900 mg IM - Q8W

Reporting group description:

In the IP of 20 weeks, participants received an oral regimen of CAB 30 mg once daily plus ABC/3TC 600/300 mg once daily. In the last 4 weeks of the IP, participants also received RPV 25 mg tablet once daily. In the MP, participants who randomized to this arm received following IMdoses: Day 1 only – CAB LA 800 mg (loading dose delivered as two 400 mg IM injections) + RPV LA 900 mg IM. Week 4 only - CAB LA 600 mg IM (second loading dose, no RPV). Week 8 - CAB LA 600 mg IM + RPV LA 900 mg IM every 8 Weeks (Q8W) for 96 weeks

Reporting group title	CAB LA 400 mg + RPV LA 600 mg IM - Q4W

Reporting group description:

In the IP of 20 weeks, participants received an oral regimen of CAB 30 mg once daily plus ABC/3TC 600/300 mg once daily. In the last 4 weeks of the IP, participants also received RPV 25 mg tablet once daily. In the MP, participants who randomized to this arm received following IM doses: Day 1 only - CAB LA 800 mg (loading dose delivered as two 400 mg IM injections) + RPV LA 600 mg IM. Week 4 - CAB LA 400 mg IM + RPV LA 600 mg IM every 4 weeks (Q4W) for 96 weeks

Reporting group title	CAB 30 mg + ABC/3TC once daily

Reporting group description:

In the IP of 20 weeks, participants received an oral regimen of CAB 30 mg once daily plus ABC/3TC 600/300 mg once daily. In the last 4 weeks of the IP, participants also received RPV 25 mg tablet once daily. In the MP, participants who randomized to this arm received an oral regimen of 30 mg of CAB and ABC/3TC once daily for 96 weeks (or 104 weeks if going on to the EP).

Serious adverse events	CAB LA 600 mg + RPV LA 900 mg IM - Q8W	CAB LA 400 mg + RPV LA 600 mg IM - Q4W	CAB 30 mg + ABC/3TC once daily
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 115 (7.83%)	8 / 115 (6.96%)	5 / 56 (8.93%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			

subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (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
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (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
Rib fracture			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (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
Epicondylitis			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mountain sickness acute			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (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
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (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
Headache			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (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

Migraine			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nerve root compression			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Allergic granulomatous angiitis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (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
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
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			
Suicide attempt			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (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
Substance abuse			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			

subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (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			
Fistula			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (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
Muscular weakness			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (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
Neck pain			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (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
Pain in extremity			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (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			
Abscess limb			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (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
Anal abscess			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (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
Epididymitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (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

Orchitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (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
Peritonsillar abscess			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (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 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (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 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	CAB LA 600 mg + RPV LA 900 mg IM - Q8W	CAB LA 400 mg + RPV LA 600 mg IM - Q4W	CAB 30 mg + ABC/3TC once daily
Total subjects affected by non-serious adverse events			
subjects affected / exposed	115 / 115 (100.00%)	113 / 115 (98.26%)	52 / 56 (92.86%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	7 / 115 (6.09%)	9 / 115 (7.83%)	2 / 56 (3.57%)
occurrences (all)	8	12	2
Skin papilloma			
subjects affected / exposed	5 / 115 (4.35%)	3 / 115 (2.61%)	1 / 56 (1.79%)
occurrences (all)	5	4	1
Benign salivary gland neoplasm			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Kaposi's sarcoma			

subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Oral papilloma			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	4 / 115 (3.48%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	4	2	0
Flushing			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Lymphoedema			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Thrombophlebitis superficial			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Dental care			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	106 / 115 (92.17%)	106 / 115 (92.17%)	0 / 56 (0.00%)
occurrences (all)	697	836	0
Injection site swelling			
subjects affected / exposed	28 / 115 (24.35%)	30 / 115 (26.09%)	0 / 56 (0.00%)
occurrences (all)	72	84	0
Injection site nodule			

subjects affected / exposed	21 / 115 (18.26%)	28 / 115 (24.35%)	0 / 56 (0.00%)
occurrences (all)	57	87	0
Injection site induration			
subjects affected / exposed	22 / 115 (19.13%)	20 / 115 (17.39%)	0 / 56 (0.00%)
occurrences (all)	53	72	0
Injection site pruritus			
subjects affected / exposed	19 / 115 (16.52%)	18 / 115 (15.65%)	0 / 56 (0.00%)
occurrences (all)	66	43	0
Injection site warmth			
subjects affected / exposed	17 / 115 (14.78%)	16 / 115 (13.91%)	0 / 56 (0.00%)
occurrences (all)	49	36	0
Fatigue			
subjects affected / exposed	11 / 115 (9.57%)	14 / 115 (12.17%)	4 / 56 (7.14%)
occurrences (all)	11	16	5
Pyrexia			
subjects affected / exposed	13 / 115 (11.30%)	11 / 115 (9.57%)	3 / 56 (5.36%)
occurrences (all)	16	11	3
Injection site bruising			
subjects affected / exposed	15 / 115 (13.04%)	10 / 115 (8.70%)	0 / 56 (0.00%)
occurrences (all)	31	20	0
Asthenia			
subjects affected / exposed	6 / 115 (5.22%)	8 / 115 (6.96%)	9 / 56 (16.07%)
occurrences (all)	8	8	10
Injection site erythema			
subjects affected / exposed	9 / 115 (7.83%)	11 / 115 (9.57%)	0 / 56 (0.00%)
occurrences (all)	19	31	0
Influenza like illness			
subjects affected / exposed	3 / 115 (2.61%)	5 / 115 (4.35%)	0 / 56 (0.00%)
occurrences (all)	4	6	0
Injection site discolouration			
subjects affected / exposed	2 / 115 (1.74%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	3	3	0
Injection site haematoma			
subjects affected / exposed	2 / 115 (1.74%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	2	13	0
Chest pain			

subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	1 / 56 (1.79%)
occurrences (all)	0	2	1
Malaise			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	1	0	1
Pain			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	2	1	0
Chest discomfort			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Cyst			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Discomfort			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Energy increased			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Feeling hot			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Injection site anaesthesia			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Injection site hypoaesthesia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Injection site inflammation			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Injection site paraesthesia			

subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Injection site rash			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Injection site reaction			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Oedema			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Secretion discharge			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Temperature intolerance			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	3 / 115 (2.61%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	3	3	0
Allergy to arthropod bite			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Hypersensitivity			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	3
Multiple allergies			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Social circumstances			
Stress at work			

subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 115 (0.87%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	1	3	0
Balanoposthitis			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	2	1	0
Genital lesion			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Haematospermia			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	3	1	0
Prostatitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Testis discomfort			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Vaginal discharge			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 115 (6.96%)	11 / 115 (9.57%)	3 / 56 (5.36%)
occurrences (all)	10	11	3
Oropharyngeal pain			
subjects affected / exposed	1 / 115 (0.87%)	5 / 115 (4.35%)	1 / 56 (1.79%)
occurrences (all)	1	6	2
Rhinitis allergic			
subjects affected / exposed	3 / 115 (2.61%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	3	3	0
Catarrh			

subjects affected / exposed	3 / 115 (2.61%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	3	2	1
Rhinorrhoea			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	2 / 56 (3.57%)
occurrences (all)	1	2	2
Nasal congestion			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	1	2	0
Sinus congestion			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	2	0	1
Allergic sinusitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Asthma			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Dysphonia			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal discomfort			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Pharyngeal erythema			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Pleuritic pain			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0

Productive cough			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	9 / 115 (7.83%)	10 / 115 (8.70%)	3 / 56 (5.36%)
occurrences (all)	9	10	3
Anxiety			
subjects affected / exposed	7 / 115 (6.09%)	10 / 115 (8.70%)	2 / 56 (3.57%)
occurrences (all)	9	14	2
Depression			
subjects affected / exposed	6 / 115 (5.22%)	6 / 115 (5.22%)	5 / 56 (8.93%)
occurrences (all)	7	8	5
Abnormal dreams			
subjects affected / exposed	2 / 115 (1.74%)	3 / 115 (2.61%)	2 / 56 (3.57%)
occurrences (all)	2	3	2
Depressed mood			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	3 / 56 (5.36%)
occurrences (all)	2	0	3
Irritability			
subjects affected / exposed	4 / 115 (3.48%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	4	0	0
Nightmare			
subjects affected / exposed	1 / 115 (0.87%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	1	3	0
Libido decreased			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	1	2	0
Affect lability			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Affective disorder			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Anxiety disorder			

subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Psychotic disorder			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	0	1	1
Abnormal behaviour			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Acute stress disorder			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Agitation			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Apathy			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Initial insomnia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Libido increased			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Mood altered			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Mood swings			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Nervousness			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Panic attack			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Paranoia			

subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Personality disorder			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Sleep disorder			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Stress			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Suicidal ideation			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Tachyphrenia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Trichotillomania			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 115 (2.61%)	3 / 115 (2.61%)	2 / 56 (3.57%)
occurrences (all)	3	3	2
Lipase increased			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	2	1	1
Transaminases increased			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	1	2	0
Blood creatinine increased			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			

subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Eosinophil count decreased			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count increased			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Weight increased			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	1 / 115 (0.87%)	4 / 115 (3.48%)	0 / 56 (0.00%)
occurrences (all)	1	4	0
Contusion			
subjects affected / exposed	0 / 115 (0.00%)	4 / 115 (3.48%)	0 / 56 (0.00%)
occurrences (all)	0	5	0
Wound			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	2 / 56 (3.57%)
occurrences (all)	1	1	2
Arthropod bite			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	2	1	0
Hand fracture			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	1	0	1
Joint injury			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Limb injury			

subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	1	0	1
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Post-traumatic pain			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	0	1	1
Tendon rupture			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Compression fracture			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Epicondylitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Exposure to communicable disease			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Foot fracture			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Injury			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Joint dislocation			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Ligament rupture			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Muscle contusion			

subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Periorbital contusion			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Procedural complication			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Rib fracture			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Scratch			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Thermal burn			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	0	1	1
Tachycardia			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Hypertensive heart disease			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Mitral valve incompetence			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Myocardial infarction			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Ventricular dyskinesia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0

Nervous system disorders			
Headache			
subjects affected / exposed	24 / 115 (20.87%)	24 / 115 (20.87%)	10 / 56 (17.86%)
occurrences (all)	25	34	13
Dizziness			
subjects affected / exposed	6 / 115 (5.22%)	6 / 115 (5.22%)	2 / 56 (3.57%)
occurrences (all)	7	7	2
Paraesthesia			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	2 / 56 (3.57%)
occurrences (all)	1	2	2
Hypersomnia			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	2	1	0
Aphonia			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Hypoaesthesia			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Migraine			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	8	0	0
Presyncope			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Sciatica			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Vagus nerve disorder			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Amnesia			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Dysaesthesia			

subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Loss of consciousness			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Memory impairment			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Nerve root compression			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Parosmia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Polyneuropathy			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Poor quality sleep			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Restless legs syndrome			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Neutropenia			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	2 / 56 (3.57%)
occurrences (all)	0	0	2

Eosinophilia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Leukocytosis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Necrotising granulomatous lymphadenitis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Anaemia			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	4 / 56 (7.14%)
occurrences (all)	0	0	4
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	2 / 56 (3.57%)
occurrences (all)	0	1	3
Vertigo			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	2	1	0
Deafness			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Tympanic membrane disorder			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Tympanic membrane perforation			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye pruritus			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	2	1	0
Conjunctivitis allergic			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Blepharitis			

subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Chalazion			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Chromatopsia			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Conjunctival haemorrhage			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Erythema of eyelid			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Keratitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Photophobia			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	23 / 115 (20.00%)	28 / 115 (24.35%)	9 / 56 (16.07%)
occurrences (all)	28	36	10
Nausea			
subjects affected / exposed	14 / 115 (12.17%)	15 / 115 (13.04%)	9 / 56 (16.07%)
occurrences (all)	16	21	11

Abdominal pain			
subjects affected / exposed	9 / 115 (7.83%)	4 / 115 (3.48%)	4 / 56 (7.14%)
occurrences (all)	10	5	4
Vomiting			
subjects affected / exposed	3 / 115 (2.61%)	7 / 115 (6.09%)	4 / 56 (7.14%)
occurrences (all)	3	9	5
Dyspepsia			
subjects affected / exposed	4 / 115 (3.48%)	7 / 115 (6.09%)	1 / 56 (1.79%)
occurrences (all)	4	7	1
Constipation			
subjects affected / exposed	4 / 115 (3.48%)	4 / 115 (3.48%)	2 / 56 (3.57%)
occurrences (all)	4	4	2
Odynophagia			
subjects affected / exposed	4 / 115 (3.48%)	2 / 115 (1.74%)	3 / 56 (5.36%)
occurrences (all)	4	4	5
Abdominal distension			
subjects affected / exposed	4 / 115 (3.48%)	3 / 115 (2.61%)	1 / 56 (1.79%)
occurrences (all)	5	3	1
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 115 (1.74%)	5 / 115 (4.35%)	0 / 56 (0.00%)
occurrences (all)	2	5	0
Haemorrhoids			
subjects affected / exposed	5 / 115 (4.35%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	6	1	1
Proctitis			
subjects affected / exposed	2 / 115 (1.74%)	2 / 115 (1.74%)	2 / 56 (3.57%)
occurrences (all)	2	3	2
Abdominal discomfort			
subjects affected / exposed	2 / 115 (1.74%)	2 / 115 (1.74%)	1 / 56 (1.79%)
occurrences (all)	2	2	1
Proctalgia			
subjects affected / exposed	4 / 115 (3.48%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	5	1	0
Abdominal pain upper			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	2	1	1

Anal fissure			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	2 / 56 (3.57%)
occurrences (all)	3	0	2
Rectal haemorrhage			
subjects affected / exposed	1 / 115 (0.87%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	1	3	0
Anogenital dysplasia			
subjects affected / exposed	3 / 115 (2.61%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	3	0	0
Flatulence			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	1	2	0
Gastritis			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	1	1	1
Oral disorder			
subjects affected / exposed	0 / 115 (0.00%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	0	3	0
Anal pruritus			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	1	0	1
Aphthous stomatitis			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Dental caries			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	0	1	1
Faeces soft			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	0	1	1
Toothache			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	0	3	3

Abdominal pain lower			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Anal ulcer			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Anorectal discomfort			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Cheilosis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Enteritis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Erosive duodenitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Food poisoning			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Gingival oedema			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Gingival pain			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Glossitis			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	2

Haemorrhoids thrombosed			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	2
Large intestine polyp			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Lip oedema			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Lip swelling			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Lip ulceration			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Loose tooth			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Noninfective gingivitis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Palatal disorder			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Perianal erythema			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Rectal discharge			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Tongue discolouration			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0

Tongue ulceration			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Umbilical hernia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Gallbladder polyp			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Hepatotoxicity			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	6 / 115 (5.22%)	6 / 115 (5.22%)	1 / 56 (1.79%)
occurrences (all)	6	7	1
Eczema			
subjects affected / exposed	5 / 115 (4.35%)	0 / 115 (0.00%)	3 / 56 (5.36%)
occurrences (all)	5	0	3
Pruritus			
subjects affected / exposed	4 / 115 (3.48%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	4	3	0
Night sweats			
subjects affected / exposed	2 / 115 (1.74%)	2 / 115 (1.74%)	1 / 56 (1.79%)
occurrences (all)	2	4	2
Skin induration			
subjects affected / exposed	2 / 115 (1.74%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	2	2	0
Urticaria			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	1 / 56 (1.79%)
occurrences (all)	1	2	1
Acne			

subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	2	1	0
Dermatitis			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	1	3	0
Dry skin			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	2	1	0
Hyperhidrosis			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	1	1	1
Intertrigo			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	2	1	0
Papule			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	2	1	0
Seborrhoeic dermatitis			
subjects affected / exposed	3 / 115 (2.61%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	3	0	0
Alopecia			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Hyperkeratosis			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Photosensitivity reaction			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	0	1	1
Rash maculo-papular			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Rosacea			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Skin lesion			

subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Alopecia areata			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Dermal cyst			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Dermatitis allergic			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Dermatitis contact			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Dyshidrotic eczema			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Hidradenitis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Nail discolouration			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Onycholysis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Penile ulceration			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Pityriasis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Psoriasis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Rash papular			

subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Rash vesicular			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Skin plaque			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 115 (1.74%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	2	3	0
Nephrolithiasis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	1	0	1
Haematuria			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Nephropathy toxic			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Renal colic			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	12 / 115 (10.43%)	7 / 115 (6.09%)	4 / 56 (7.14%)
occurrences (all)	12	8	5
Myalgia			
subjects affected / exposed	6 / 115 (5.22%)	5 / 115 (4.35%)	1 / 56 (1.79%)
occurrences (all)	7	5	1
Arthralgia			
subjects affected / exposed	4 / 115 (3.48%)	4 / 115 (3.48%)	2 / 56 (3.57%)
occurrences (all)	5	4	2
Pain in extremity			

subjects affected / exposed	3 / 115 (2.61%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	3	3	0
Musculoskeletal pain			
subjects affected / exposed	4 / 115 (3.48%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	4	1	0
Muscle spasms			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	2	1	1
Musculoskeletal chest pain			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	2	1	1
Neck pain			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	1 / 56 (1.79%)
occurrences (all)	1	2	1
Musculoskeletal stiffness			
subjects affected / exposed	3 / 115 (2.61%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	3	0	0
Chondropathy			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	2 / 56 (3.57%)
occurrences (all)	0	0	2
Groin pain			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	0	1	1
Muscle contracture			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	1	0	1
Dactylitis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Extremity contracture			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Finger deformity			

subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Fistula			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Joint effusion			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Osteoarthritis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Osteochondrosis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Osteoporosis			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Rotator cuff syndrome			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Synovial cyst			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Tenosynovitis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	27 / 115 (23.48%)	32 / 115 (27.83%)	15 / 56 (26.79%)
occurrences (all)	36	44	22
Upper respiratory tract infection			
subjects affected / exposed	18 / 115 (15.65%)	9 / 115 (7.83%)	3 / 56 (5.36%)
occurrences (all)	23	9	3

Syphilis			
subjects affected / exposed	10 / 115 (8.70%)	8 / 115 (6.96%)	3 / 56 (5.36%)
occurrences (all)	10	10	3
Gastroenteritis			
subjects affected / exposed	7 / 115 (6.09%)	10 / 115 (8.70%)	3 / 56 (5.36%)
occurrences (all)	7	11	3
Bronchitis			
subjects affected / exposed	8 / 115 (6.96%)	6 / 115 (5.22%)	4 / 56 (7.14%)
occurrences (all)	9	6	4
Pharyngitis			
subjects affected / exposed	9 / 115 (7.83%)	6 / 115 (5.22%)	1 / 56 (1.79%)
occurrences (all)	9	6	1
Influenza			
subjects affected / exposed	6 / 115 (5.22%)	9 / 115 (7.83%)	0 / 56 (0.00%)
occurrences (all)	6	9	0
Respiratory tract infection			
subjects affected / exposed	4 / 115 (3.48%)	5 / 115 (4.35%)	6 / 56 (10.71%)
occurrences (all)	4	5	7
Gonorrhoea			
subjects affected / exposed	7 / 115 (6.09%)	5 / 115 (4.35%)	0 / 56 (0.00%)
occurrences (all)	11	6	0
Rhinitis			
subjects affected / exposed	3 / 115 (2.61%)	4 / 115 (3.48%)	3 / 56 (5.36%)
occurrences (all)	3	4	3
Tonsillitis			
subjects affected / exposed	4 / 115 (3.48%)	4 / 115 (3.48%)	2 / 56 (3.57%)
occurrences (all)	4	5	2
Oral herpes			
subjects affected / exposed	2 / 115 (1.74%)	5 / 115 (4.35%)	2 / 56 (3.57%)
occurrences (all)	7	5	4
Sinusitis			
subjects affected / exposed	4 / 115 (3.48%)	2 / 115 (1.74%)	3 / 56 (5.36%)
occurrences (all)	4	2	4
Urethritis			
subjects affected / exposed	3 / 115 (2.61%)	6 / 115 (5.22%)	0 / 56 (0.00%)
occurrences (all)	5	6	0

Conjunctivitis			
subjects affected / exposed	3 / 115 (2.61%)	2 / 115 (1.74%)	3 / 56 (5.36%)
occurrences (all)	3	2	3
Pharyngotonsillitis			
subjects affected / exposed	6 / 115 (5.22%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	7	1	1
Cellulitis			
subjects affected / exposed	3 / 115 (2.61%)	4 / 115 (3.48%)	0 / 56 (0.00%)
occurrences (all)	3	4	0
Chlamydial infection			
subjects affected / exposed	4 / 115 (3.48%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	4	3	0
Folliculitis			
subjects affected / exposed	6 / 115 (5.22%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	7	1	0
Ear infection			
subjects affected / exposed	3 / 115 (2.61%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	3	4	0
Genital herpes			
subjects affected / exposed	6 / 115 (5.22%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	7	0	0
Tinea pedis			
subjects affected / exposed	2 / 115 (1.74%)	3 / 115 (2.61%)	1 / 56 (1.79%)
occurrences (all)	2	3	1
Viral infection			
subjects affected / exposed	2 / 115 (1.74%)	2 / 115 (1.74%)	2 / 56 (3.57%)
occurrences (all)	3	2	2
Hordeolum			
subjects affected / exposed	1 / 115 (0.87%)	3 / 115 (2.61%)	1 / 56 (1.79%)
occurrences (all)	1	3	1
Pharyngitis streptococcal			
subjects affected / exposed	2 / 115 (1.74%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	2	4	0
Subcutaneous abscess			
subjects affected / exposed	3 / 115 (2.61%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	3	2	0

Tooth infection			
subjects affected / exposed	2 / 115 (1.74%)	3 / 115 (2.61%)	0 / 56 (0.00%)
occurrences (all)	2	3	0
Acute sinusitis			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	2	1	1
Gingivitis			
subjects affected / exposed	3 / 115 (2.61%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	3	0	1
Herpes zoster			
subjects affected / exposed	0 / 115 (0.00%)	4 / 115 (3.48%)	0 / 56 (0.00%)
occurrences (all)	0	4	0
Lymphogranuloma venereum			
subjects affected / exposed	2 / 115 (1.74%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	2	3	0
Acute hepatitis C			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	1 / 56 (1.79%)
occurrences (all)	0	2	1
Fungal infection			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	2	0	1
Furuncle			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	1	1	1
Gastroenteritis viral			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	2 / 56 (3.57%)
occurrences (all)	0	1	2
Hepatitis C			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	1	3	0
Proctitis chlamydial			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	2	1	0
Secondary syphilis			
subjects affected / exposed	3 / 115 (2.61%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	3	1	0

Tinea versicolour			
subjects affected / exposed	1 / 115 (0.87%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	1	3	0
Urinary tract infection			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	1 / 56 (1.79%)
occurrences (all)	0	2	1
Acarodermatitis			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	3	0	0
Anal chlamydia infection			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	3	0	0
Cystitis			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	0	3	0
Enterobiasis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	0	1	1
Fungal skin infection			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Giardiasis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	0	1	1
Herpes simplex			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	2	1	0
Herpes virus infection			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	5	0	0
Lung infection			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	0	1	1
Onychomycosis			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	2 / 56 (3.57%)
occurrences (all)	0	0	2

Pneumonia			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Oropharyngeal gonococcal infection			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
Skin infection			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	4	2	0
Tooth abscess			
subjects affected / exposed	0 / 115 (0.00%)	2 / 115 (1.74%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 115 (1.74%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	2	0	0
AIDS dementia complex			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Abscess			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Abscess limb			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Acute tonsillitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Anal infection			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Anorectal human papilloma virus			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Blastocystis infection			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0

Body tinea			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Bronchitis bacterial			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Carbuncle			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Cervicitis			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Chronic sinusitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Cryptosporidiosis infection			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Diarrhoea infectious			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Epididymitis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Eye infection			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis norovirus			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0

Genital infection bacterial			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Haemophilus infection			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Hepatitis syphilitic			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Herpes ophthalmic			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Impetigo			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Infection			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Injection site abscess			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Lice infestation			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	2
Molluscum contagiosum			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0

Osteomyelitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Otitis externa			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Pilonidal cyst			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Proctitis gonococcal			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection bacterial			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Rhinovirus infection			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Shigella infection			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Spirochaetal infection			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Tracheobronchitis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Urethritis chlamydial			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0

Urethritis gonococcal			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Viral tonsillitis			
subjects affected / exposed	0 / 115 (0.00%)	0 / 115 (0.00%)	1 / 56 (1.79%)
occurrences (all)	0	0	1
Visceral leishmaniasis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Vulvovaginitis trichomonal			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	2 / 115 (1.74%)	4 / 115 (3.48%)	1 / 56 (1.79%)
occurrences (all)	3	4	1
Decreased appetite			
subjects affected / exposed	3 / 115 (2.61%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	4	1	0
Vitamin D deficiency			
subjects affected / exposed	2 / 115 (1.74%)	1 / 115 (0.87%)	1 / 56 (1.79%)
occurrences (all)	2	1	1
Hypertriglyceridaemia			
subjects affected / exposed	1 / 115 (0.87%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Carbohydrate intolerance			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (0.00%)
occurrences (all)	1	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Glucose tolerance impaired			

subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Increased appetite			
subjects affected / exposed	0 / 115 (0.00%)	1 / 115 (0.87%)	0 / 56 (0.00%)
occurrences (all)	0	1	0
Vitamin B complex deficiency			
subjects affected / exposed	1 / 115 (0.87%)	0 / 115 (0.00%)	0 / 56 (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
28 October 2013	Amendment 1: was finalized 28 October 2013, however, was never implemented due to a design change requiring a second amendment. Amendment 1 was prepared to address the following changes: universal changes to naming conventions for the long acting formulation of CAB, simplifying the protocol summary to allow better understanding of the protocol, clarifying the study schematic to increase understanding, clarification the purpose of and analyses to be performed by the Independent Data Monitoring Committee to reflect current plans, clarification of the intent of the Day 1 analysis as a possible analysis if needed, clarification to study treatments including the addition of the ingredients of the long acting formulations of both study treatments, clarification of health outcomes objectives, timings and questionnaires, adding the assessment of exercises habits and intravenous drug use, removing some assessments to simplify study visits, updates and simplification to the time and events tables and additional miscellaneous clarifications.
23 January 2014	Amendment No.02: Primary modifications included, Study design adapted to consolidate the Induction Period into a single 20 Week arm and for the addition of an every 8 week IM regimen into the Maintenance Period. Increased sample size to 265 subjects. Primary endpoint changed from Week 24 to Week 32. Dose rationale updated.
13 June 2014	Amendment No.03: Primary modifications included, ABC/3TC added as Investigational Product beginning at Day 1 of the Maintenance Period; clarification that alternative background therapy (if positive for HLA-B*5701) is not counted as the protocol permitted switch for NRTI; clarification regarding provision of alternative NRTI therapy; change in visit window for subjects on the oral dosing arm; excursion temperatures added for ABC/3TC and RPV oral tablet; text added for ABC/3TC overdose; deleted option for participant informed consent by legal representative; Time and Events Table clarifications. Additional clarifications and typographical corrections throughout.
22 April 2015	Amendment No. 4: Primary modifications included, addition of a 2-hour post dose pharmacokinetic samples and electrocardiogram at Week 32 and Week 48 for subjects receiving intramuscular CAB LA and RPV LA; addition of LAI116482 Week 96 data; addition of maladministration of injection risk; additional clarifications for injection site reaction collection; clarified visit windows.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported