Clinical trial results:
A Phase III, randomized, multicenter, open-label, non-inferiority study evaluating the efficacy, safety and tolerability of switching to dolutegravir/lamivudine fixed dose combination in HIV-1 infected adults who are virologically suppressed

Summary

EudraCT number	2018-000177-72
Trial protocol	GB SE DE FR DK ES IT
Global end of trial date	

Results information

Result version number	v2
This version publication date	29 June 2022
First version publication date	04 May 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	208090

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04021290
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, ViiV Healthcare, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, ViiV Healthcare, 1 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	23 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 April 2021
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study is to demonstrate the non-inferior antiviral activity of switching to DTG/3TC FDC once daily compared to continuation of CAR over 48 weeks in virologically suppressed adults living with HIV-1.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 November 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 26
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Brazil: 39
Country: Number of subjects enrolled	Canada: 20
Country: Number of subjects enrolled	China: 38
Country: Number of subjects enrolled	Denmark: 15
Country: Number of subjects enrolled	France: 39
Country: Number of subjects enrolled	Germany: 40
Country: Number of subjects enrolled	Italy: 37
Country: Number of subjects enrolled	Mexico: 27
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	South Africa: 18
Country: Number of subjects enrolled	Spain: 44
Country: Number of subjects enrolled	Sweden: 11
Country: Number of subjects enrolled	Taiwan: 23
Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	United States: 64
Worldwide total number of subjects	493
EEA total number of subjects	198

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)	467
From 65 to 84 years	26
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants in the DTG/3TC FDC arm will enter the continuation phase (following week 52) for which data collection is still ongoing and additional results will be provided after study completion. However, participants in the CAR arm have completed the study and no additional results will be available.

Pre-assignment

Screening details:

The results presented are based on the primary analysis. A total of 493 adult participants were enrolled in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Participants who received DTG/3TC FDC

Arm description:

Eligible participants were randomized to receive 50 milligrams (mg)/300 mg DTG/3TC FDC therapy from day 1 up to 52 weeks. Participants who complete 52 weeks of treatment will have the opportunity to continue receiving DTG/3TC FDC once daily in the continuation phase.

Arm type	Experimental
Investigational medicinal product name	Dolutegravir (DTG)+Lamivudine (3TC) fixed dose combination (FDC)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received DTG 50 milligrams (mg) + 3TC 300 mg FDC as a white, oval and film-coated tablet. The tablets were packed in high density polyethylene (HDPE) bottles with induction seals, 2 grams (gm) desiccant, and child resistant closures. Each 60 milliliter (mL) bottle contains 30 tablets.

Arm title	Participants who received CAR

Arm description:

Eligible participants received CAR from day 1 up to 52 weeks. CAR included 2 nucleoside reverse transcriptase inhibitors (NTRIs) plus either an integrase inhibitor (INI), non-nucleoside reverse transcriptase inhibitor (NNRTI), or boosted protease inhibitor (PI) or atazanavir unboosted

Arm type	Active comparator
Investigational medicinal product name	CAR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CAR will include 2 NTRIs plus either an INI, NNRTI, or boosted PI or atazanavir unboosted.

Number of subjects in period 1	Participants who received DTG/3TC FDC	Participants who received CAR
Started	246	247
Completed	143	229
Not completed	103	18
Physician decision	1	2
Consent withdrawn by subject	1	5
Adverse event, non-fatal	4	3
Protocol Deviation	5	4
Death	1	-
Ongoing	89	-
Lost to follow-up	2	1
Lack of efficacy	-	3

Baseline characteristics

Reporting groups	
Reporting group title	Participants who received DTG/3TC FDC
Reporting group description:	
Eligible participants were randomized to receive 50 milligrams (mg)/300 mg DTG/3TC FDC therapy from day 1 up to 52 weeks. Participants who complete 52 weeks of treatment will have the opportunity to continue receiving DTG/3TC FDC once daily in the continuation phase.	
Reporting group title	Participants who received CAR
Reporting group description:	
Eligible participants received CAR from day 1 up to 52 weeks. CAR included 2 nucleoside reverse transcriptase inhibitors (NTRIs) plus either an integrase inhibitor (INI), non-nucleoside reverse transcriptase inhibitor (NNRTI), or boosted protease inhibitor (PI) or atazanavir unboosted	

Reporting group values	Participants who received DTG/3TC FDC	Participants who received CAR	Total
Number of subjects	246	247	493
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	237	230	467
From 65-84 years	9	17	26
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	45.5	45.8	
standard deviation	± 11.04	± 11.99	-
Sex: Female, Male Units: Participants			
Female	108	84	192
Male	138	163	301
Race/Ethnicity, Customized Units: Subjects			
African American/African Heritage	45	48	93
American Indian OR Alaska Native	18	14	32
Asian - East Asian Heritage	27	36	63
Asian - South East Asian Heritage	4	3	7
White - Arabic/North African Heritage	7	4	11
White - White/Caucasian/European Heritage	142	140	282
Multiple	3	2	5

End points

End points reporting groups

Reporting group title	Participants who received DTG/3TC FDC

Reporting group description:

Eligible participants were randomized to receive 50 milligrams (mg)/300 mg DTG/3TC FDC therapy from day 1 up to 52 weeks. Participants who complete 52 weeks of treatment will have the opportunity to continue receiving DTG/3TC FDC once daily in the continuation phase.

Reporting group title	Participants who received CAR

Reporting group description:

Eligible participants received CAR from day 1 up to 52 weeks. CAR included 2 nucleoside reverse transcriptase inhibitors (NTRIs) plus either an integrase inhibitor (INI), non-nucleoside reverse transcriptase inhibitor (NNRTI), or boosted protease inhibitor (PI) or atazanavir unboosted

Primary: Number of participants with plasma HIV-1 Ribonucleic acid (RNA) >=50 copies/milliliter (c/mL) as per Food and Drug Administration (FDA) snapshot category at Week 48

End point title	Number of participants with plasma HIV-1 Ribonucleic acid (RNA) >=50 copies/milliliter (c/mL) as per Food and Drug Administration (FDA) snapshot category at Week 48

End point description:

Number of participants with plasma HIV 1 RNA >=50 c/mL were evaluated using FDA snapshot algorithm at Week 48 to demonstrate the non-inferior antiviral activity of switching to DTG/3TC FDC once daily compared to continuation of CAR over 48 weeks. The FDA snapshot algorithm defines a participant's virologic response status using only the viral load at the predefined time point within a window of time (HIV-RNA equal to or above 50 copies/mL and HIV-RNA below 50 copies/mL), along with study drug discontinuation status. Participants with plasma HIV 1 RNA >=50 c/mL were termed as subjects with virologic failure. The third category of the FDA snapshot ("No virologic data") is not pre-defined as an endpoint and therefore not reported separately. Intent To Treat-Exposed (ITT-E) population included all randomized participants who received at least one dose of study medication either DTG/3TC or CAR.

End point type	Primary

End point timeframe:

Week 48

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	247		
Units: Participants	1	3		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Participants who received DTG/3TC FDC v Participants who received CAR

Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted Difference in Percent (ADP)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	0.8

Secondary: Number of participants with plasma HIV-1 RNA <50 c/mL using the FDA Snapshot algorithm at Week 48

End point title	Number of participants with plasma HIV-1 RNA <50 c/mL using the FDA Snapshot algorithm at Week 48

End point description:

Number of participants with plasma HIV 1 RNA <50 c/mL were evaluated using FDA snapshot algorithm at Week 48 to demonstrate the antiviral activity of switching to DTG/3TC FDC once daily compared to continuation of CAR over 48 weeks. The FDA snapshot algorithm defines a participant's virologic response status using only the viral load at the predefined time point within a window of time (HIV-RNA equal to or above 50 copies/mL and HIV-RNA below 50 copies/mL), along with study drug discontinuation status. Participants with plasma HIV 1 RNA <50 c/mL were termed as subjects with virologic success. The third category of the FDA snapshot ("No virologic data") is not pre-defined as an endpoint and therefore not reported separately. Intent To Treat-Exposed.

End point type	Secondary

End point timeframe:

Week 48

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	247		
Units: Participants	232	229		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Participants who received DTG/3TC FDC v Participants who received CAR
Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted Difference in Percent
Point estimate	1.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	5.9

Secondary: Number of participants with plasma HIV-1 RNA >=50 c/mL as per FDA snapshot category at Week 24

End point title	Number of participants with plasma HIV-1 RNA >=50 c/mL as per FDA snapshot category at Week 24

End point description:

Number of participants with plasma HIV 1 RNA >=50 c/mL were evaluated using FDA snapshot algorithm at Week 24 to demonstrate the antiviral activity of switching to DTG/3TC FDC once daily compared to continuation of CAR over 24 weeks. The FDA snapshot algorithm defines a participant's virologic response status using only the viral load at the predefined time point within a window of time (HIV-RNA equal to or above 50 copies/mL and HIV-RNA below 50 copies/mL), along with study drug discontinuation status. Participants with plasma HIV 1 RNA >=50 c/mL were termed as subjects with virologic failure. The third category of the FDA snapshot ("No virologic data") is not pre-defined as an endpoint and therefore not reported separately. Intent To Treat-Exposed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	247		
Units: Participants	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with plasma HIV-1 RNA <50 c/mL using the FDA Snapshot algorithm at Week 24

End point title	Number of participants with plasma HIV-1 RNA <50 c/mL using the FDA Snapshot algorithm at Week 24

End point description:

Number of participants with plasma HIV 1 RNA <50 c/mL were evaluated using FDA snapshot algorithm at Week 24 to demonstrate the antiviral activity of switching to DTG/3TC FDC once daily compared to continuation of CAR over 24 weeks. The FDA snapshot algorithm defines a participant's virologic response status using only the viral load at the predefined time point within a window of time (HIV-RNA equal to or above 50 copies/mL and HIV-RNA below 50 copies/mL), along with study drug discontinuation status. Participants with plasma HIV 1 RNA <50 c/mL were termed as subjects with virologic success. The third category of the FDA snapshot ("No virologic data") is not pre-defined as an endpoint and therefore not reported separately. Intent To Treat-Exposed.

End point type	Secondary

End point timeframe:

Week 24

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	247		
Units: Participants	234	237		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in cluster of differentiation 4 (CD4+) cell count for Week 24

End point title	Change from Baseline in cluster of differentiation 4 (CD4+) cell count for Week 24

End point description:

CD4+ cells are type of white blood cells that fight infection and as HIV infection progresses, the number of these cells declines. Baseline value is defined as the latest pre-dose assessment with a non-missing value (Day 1). Change from Baseline is defined as post-dose visit value minus Baseline value. Lymphocyte subsets were collected for assessment of this outcome measure by flow cytometry. Change from Baseline in CD4+ lymphocyte count was assessed at Week 24 to evaluate the immune effects of DTG/3TC FDC once daily compared to continuation of CAR. Plasma samples for lymphocyte subsets were collected. Intent To Treat-Exposed. Only those participants with data available at specified time points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	232	235		
Units: cells/cubic millimeter (cells/mm^3)				
median (inter-quartile range (Q1-Q3))	30.5 (-71.5 to 111)	10 (-79 to 95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4+ cell count for Week 48

End point title	Change from Baseline in CD4+ cell count for Week 48

End point description:

CD4+ cells are type of white blood cells that fight infection and as HIV infection progresses, the number of these cells declines. Baseline value is defined as the latest pre-dose assessment with a non-missing value (Day 1). Change from Baseline is defined as post-dose visit value minus Baseline value. Lymphocyte subsets were collected for assessment of this outcome measure by flow cytometry. Change from Baseline in CD4+ lymphocyte count was assessed at Week 48 to evaluate the immune effects of DTG/3TC FDC once daily compared to continuation of CAR. Plasma samples for lymphocyte subsets were collected. Intent To Treat-Exposed. Only those participants with data available at specified time points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 48

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	232	227		
Units: cells/mm^3				
median (inter-quartile range (Q1-Q3))	30 (-83 to 115.5)	2 (-105 to 94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4+/ cluster of differentiation 8 (CD8+) cell counts ratio for Week 24

End point title	Change from Baseline in CD4+/ cluster of differentiation 8 (CD8+) cell counts ratio for Week 24

End point description:

CD4+/CD8+ cells are type of white blood cells that fight infection and as HIV infection progresses, the number of these cells declines. Baseline value is defined as the latest pre-dose assessment with a non-missing value (Day 1). Change from Baseline is defined as post-dose visit value minus Baseline value. Lymphocyte subsets were collected for assessment of this outcome measure by flow cytometry. Change from Baseline in CD4+/CD8+ lymphocyte cell count ratio was assessed at Week 24 to evaluate the immune effects of DTG/3TC FDC once daily compared to continuation of CAR. Plasma samples for lymphocyte subsets were collected. Intent To Treat-Exposed. Only those participants with data available at specified time points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	232	235		
Units: Ratio				
median (inter-quartile range (Q1-Q3))	-0.02 (-0.105 to 0.07)	0.01 (-0.06 to 0.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4+/CD8+ cell counts ratio for Week 48

End point title	Change from Baseline in CD4+/CD8+ cell counts ratio for Week 48

End point description:

CD4+/CD8+ cells are type of white blood cells that fight infection and as HIV infection progresses, the number of these cells declines. Baseline value is defined as the latest pre-dose assessment with a non-missing value (Day 1). Change from Baseline is defined as post-dose visit value minus Baseline value. Lymphocyte subsets were collected for assessment of this outcome measure by flow cytometry. Change from Baseline in CD4+/CD8+ lymphocyte cell count ratio was assessed at Week 48 to evaluate the immune effects of DTG/3TC FDC once daily compared to continuation of CAR. Plasma samples for lymphocyte subsets were collected. Intent To Treat-Exposed. Only those participants with data available at specified time points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 48

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	232	227		
Units: Ratio				
median (inter-quartile range (Q1-Q3))	0.04 (-0.06 to 0.13)	0.05 (-0.06 to 0.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Disease Progression through Week 24

End point title	Number of participants with Disease Progression through Week 24

End point description:

Partcipants with disease progression included incidences of HIV-associated conditions, Aquired Immuno Deficiency Syndrome (AIDS) and death. HIV-associated conditions were assessed according to the 2014 HIV infection by Centers for Disease Control and Prevention (CDC) classification system for HIV Infection

in adults to evaluate the immune effects of DTG /3TC FDC once daily compared to continuation of CAR. Intent To Treat-Exposed.

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	247		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events (AEs) and AEs leading to discontinuation

End point title	Number of participants with adverse events (AEs) and AEs leading to discontinuation

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. Safety population included all randomized participants who received at least 1 dose of study intervention either DTG/3TC or CAR.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	247		
Units: Participants				
AEs	180	172		
AEs leading to discontinuation	5	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Disease Progression through Week 48

End point title	Number of participants with Disease Progression through Week 48

End point description:

Partcipants with disease progression included incidences of HIV-associated conditions, AIDS and death. HIV-associated conditions were assessed according to the 2014 HIV infection by CDC classification system for HIV Infection in adults to evaluate the immune effects of DTG /3TC FDC once daily compared to continuation of CAR. Intent To Treat-Exposed.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	247		
Units: Participants	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With AEs by Severity Grades

End point title	Number of Participants With AEs by Severity Grades

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. AEs were evaluated by the investigator and graded according to the Division of Acquired Immunodeficiency Syndrome (DAIDS) toxicity scales from Grade 1 to 5 (1=Mild, 2=Moderate, 3=Severe, 4=Potentially life threatening, 5=Death). The higher the grade, the more severe the symptoms. Safety population included all randomized participants who received at least 1 dose of study intervention either DTG/3TC or CAR.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	247		
Units: Participants				
Grade 1	92	67		
Grade 2	77	86		
Grade 3	10	17		
Grade 4	0	2		
Grade 5	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Hepatobiliary Abnormalities through 52 weeks

End point title	Number of participants with Hepatobiliary Abnormalities through 52 weeks

End point description:

Blood samples were collected to evaluate hepatobiliary abnormalities. Number of participants with Bilirubin (BIL), Alkaline phosphatase (ALP), Alanine Aminotransferase (ALT)/combination of these with levels more than the defined hepatobiliary abnormality criteria were presented. Hepatocellular injury is defined as ([ALT/ALT ULN]/[ALP/ALP ULN]) >= 5 and ALT >=3*ULN. Safety population.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	247		
Units: Participants				
ALT >=3xUpper Limit of Normal (ULN) & BIL >=2xULN	0	0		
ALT >=3xULN & ALP <2xULN & BIL >=2xULN	0	0		
ALT >=3xULN & BIL >=1.5xULN	0	0		
AST >=3xULN & BIL >=2xULN	0	0		
AST >=3xULN & ALP <2xULN & BIL >=2xULN	0	0		
AST >=3xULN & BIL >=1.5xULN	0	0		
ALT+AST >=20xULN	0	0		
ALT+AST >=10xULN	0	0		
ALT+AST >=5xULN	0	0		
ALT+AST >=3xULN	3	2		
ALT >=20xULN	0	0		
ALT >=10xULN	0	0		
ALT >=5xULN	1	1		
ALT >=3xULN	6	5		
AST >=20xULN	0	0		
AST >=10xULN	0	0		
AST >=5xULN	1	0		
AST >=3xULN	5	2		
BIL >=2xULN	0	5		

BIL >=1.5xULN	0	7		
ALP >=1.5xULN	4	8		
ALT >=3xULN - <5xULN	5	4		
ALT >=5xULN - <10xULN	1	1		
ALT >=10xULN - <20xULN	0	0		
Hepatocellular injury	5	1		
Hepatocellular injury and BIL >=2xULN	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any AEs and AEs by severity grades for those participants with baseline creatinine clearance of 30-49 mL/min/1.73m^2

End point title	Number of participants with any AEs and AEs by severity grades for those participants with baseline creatinine clearance of 30-49 mL/min/1.73m^2

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. Number of participants with any AE were presented and AEs were graded according to the DAIDS toxicity scales from Grade 1 to 5 (1=Mild, 2=Moderate, 3=Severe, 4=Potentially life threatening, 5=Death). The higher the grade, the more severe the symptoms. Safety population. Only those participants with data available at specified time points were analyzed.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	4		
Units: Participants				
Any Event	1	3		
Grade 1	1	1		
Grade 2	0	2		
Grade 3	0	0		
Grade 4	0	0		
Grade 5	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with any AEs Leading to Discontinuation Based on Baseline Creatinine Clearance of 30-49 mL/min/1.73m^2

End point title	Number of Participants with any AEs Leading to Discontinuation Based on Baseline Creatinine Clearance of 30-49 mL/min/1.73m^2

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. Safety population. Only those participants with data available at specified time points were analyzed.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	4		
Units: Participants	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any AEs and AEs by severity grades for those participants with baseline creatinine clearance of >=50 mL/min/1.73m^2

End point title	Number of participants with any AEs and AEs by severity grades for those participants with baseline creatinine clearance of >=50 mL/min/1.73m^2

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. Number of participants with any AE were presented and AEs were graded according to the DAIDS toxicity scales from Grade 1 to 5 (1=Mild, 2=Moderate, 3=Severe, 4=Potentially life threatening, 5=Death). The higher the grade, the more severe the symptoms. Safety Population. Only those participants with data available at specified time points were analyzed.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	243		
Units: Participants				
Any Event	179	169		
Grade 1	91	66		
Grade 2	77	84		
Grade 3	10	17		

Grade 4	0	2		
Grade 5	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with any AEs Leading to Discontinuation Based on Baseline Creatinine Clearance of >=50 mL/min/1.73m^2

End point title	Number of Participants with any AEs Leading to Discontinuation Based on Baseline Creatinine Clearance of >=50 mL/min/1.73m^2

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. Safety population. Only those participants with data available at specified time points were analyzed.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	243		
Units: Participants	5	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Hepatobiliary Abnormalities through 52 Weeks Based on Baseline Creatinine Clearance of 30-49 mL/min/1.73m^2

End point title	Number of Participants with Hepatobiliary Abnormalities through 52 Weeks Based on Baseline Creatinine Clearance of 30-49 mL/min/1.73m^2

End point description:

Blood samples were collected to evaluate hepatobiliary abnormalities. Number of participants with Bilirubin (BIL), Alkaline phosphatase (ALP), Alanine Aminotransferase (ALT)/combination of these with levels more than the defined hepatobiliary abnormality criteria were presented. Hepatocellular injury is defined as ([ALT/ALT ULN]/[ALP/ALP ULN]) >= 5 and ALT >=3xULN. Safety population. Only those participants with data available at specified time points were analyzed.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	4		
Units: Participants				
ALT >=3xUpper Limit of Normal (ULN) & BIL >=2xULN	0	0		
ALT >=3xULN & ALP <2xULN & BIL >=2xULN	0	0		
ALT >=3xULN & BIL >=1.5xULN	0	0		
AST >=3xULN & BIL >=2xULN	0	0		
AST >=3xULN & ALP <2xULN & BIL >=2xULN	0	0		
AST >=3xULN & BIL >=1.5xULN	0	0		
ALT+AST >=20xULN	0	0		
ALT+AST >=10xULN	0	0		
ALT+AST >=5xULN	0	0		
ALT+AST >=3xULN	0	0		
ALT >=20xULN	0	0		
ALT >=10xULN	0	0		
ALT >=5xULN	0	0		
ALT >=3xULN	0	0		
AST >=20xULN	0	0		
AST >=10xULN	0	0		
AST >=5xULN	0	0		
AST >=3xULN	0	0		
BIL >=2xULN	0	1		
BIL >=1.5xULN	0	1		
ALP >=1.5xULN	0	0		
ALT >=3xULN - <5xULN	0	0		
ALT >=5xULN - <10xULN	0	0		
ALT >=10xULN - <20xULN	0	0		
Hepatocellular injury	0	0		
Hepatocellular injury and BIL >=2xULN	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Hepatobiliary Abnormalities through 52 Weeks Based on Baseline Creatinine Clearance of >=50 mL/min/1.73m^2

End point title	Number of Participants with Hepatobiliary Abnormalities through 52 Weeks Based on Baseline Creatinine Clearance of >=50 mL/min/1.73m^2

End point description:

Blood samples were collected to evaluate hepatobiliary abnormalities. Number of participants with Bilirubin (BIL), Alkaline phosphatase (ALP), Alanine Aminotransferase (ALT)/combination of these with

levels more than the defined hepatobiliary abnormality criteria were presented. Hepatocellular injury is defined as ([ALT/ALT ULN]/[ALP/ALP ULN]) >= 5 and ALT >=3xULN. Safety population. Only those participants with data available at specified time points were analyzed

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	243		
Units: Participants				
ALT >=3xUpper Limit of Normal (ULN) & BIL >=2xULN	0	0		
ALT >=3xULN & ALP <2xULN & BIL >=2xULN	0	0		
ALT >=3xULN & BIL >=1.5xULN	0	0		
AST >=3xULN & BIL >=2xULN	0	0		
AST >=3xULN & ALP <2xULN & BIL >=2xULN	0	0		
AST >=3xULN & BIL >=1.5xULN	0	0		
ALT+AST >=20xULN	0	0		
ALT+AST >=10xULN	0	0		
ALT+AST >=5xULN	0	0		
ALT+AST >=3xULN	3	2		
ALT >=20xULN	0	0		
ALT >=10xULN	0	0		
ALT >=5xULN	1	1		
ALT >=3xULN	6	5		
AST >=20xULN	0	0		
AST >=10xULN	0	0		
AST >=5xULN	1	0		
AST >=3xULN	5	2		
BIL >=2xULN	0	4		
BIL >=1.5xULN	0	6		
ALP >=1.5xULN	4	8		
ALT >=3xULN - <5xULN	5	4		
ALT >=5xULN - <10xULN	1	1		
ALT >=10xULN - <20xULN	0	0		
Hepatocellular injury	5	1		
Hepatocellular injury and BIL >=2xULN	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in fasting lipids at Week 24

End point title	Change from Baseline in fasting lipids at Week 24

End point description:

Lipid parameters included total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol and triglycerides. Safety Population. Only those participants with data available at specified time points has been analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	168		
Units: milligram/deciliter (mg/dL)				
arithmetic mean (standard deviation)				
Serum or Plasma Triglycerides (mg/dL)	-4.944 (± 56.4947)	-3.571 (± 61.9494)		
Serum or Plasma HDL Cholesterol, Direct (mg/dL)	-0.326 (± 9.1737)	0.585 (± 8.3277)		
Serum or Plasma Cholesterol (mg/dL)	-3.096 (± 31.6634)	0.058 (± 25.8019)		
Serum/Plasma LDL Cholesterol (Calculated, Direct)	-1.64 (± 25.5153)	-0.06 (± 19.802)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in fasting lipids at Week 48

End point title	Change from Baseline in fasting lipids at Week 48

End point description:

Lipid parameters included total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides. Safety Population. Only those participants with data available at specified time points has been analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 48

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	186	159		
Units: mg/dL				
arithmetic mean (standard deviation)				
Serum or Plasma Triglycerides (mg/dL)	-3.112 (± 66.9065)	-4.002 (± 71.0132)		

Serum or Plasma HDL Cholesterol, Direct (mg/dL)	-0.809 (± 10.5651)	0.688 (± 8.5584)		
Serum or Plasma Cholesterol (mg/dL)	0.131 (± 30.271)	2.668 (± 27.0351)		
Serum/Plasma LDL Cholesterol (Calculated, Direct)	1.753 (± 22.8585)	2.734 (± 20.0256)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with observed genotypic and phenotypic resistance to antiretrovirals (ARVs) for participants meeting confirmed virologic withdrawal (CVW) criteria

End point title	Number of participants with observed genotypic and phenotypic resistance to antiretrovirals (ARVs) for participants meeting confirmed virologic withdrawal (CVW) criteria

End point description:

Genotypic and phenotypic testing was conducted for participants who met the confirmed virologic withdrawal criteria, i.e., one assessment with HIV-1 RNA ≥200 c/mL after Day 1 with an immediately prior HIV-1 RNA ≥50 c/mL at any point in the study. Confirmed Virologic Withdrawal (CVW) population. No participants met the CVW criteria over 48 weeks; therefore, the genotypic and phenotypic resistance virologic analyses were not assessed.

End point type	Secondary

End point timeframe:

Up to week 48

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[1]	0[2]		
Units: Participants				

Notes:

[1] - No participants met the CVW criteria over 48 weeks, hence the virologic analyses were not assessed.
[2] - No participants met the CVW criteria over 48 weeks, hence the virologic analyses were not assessed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in health status by HIV Treatment Satisfaction Questionnaire (TSQ) at Week 24

End point title	Change from Baseline in health status by HIV Treatment Satisfaction Questionnaire (TSQ) at Week 24

End point description:

The HIV Treatment Satisfaction Questionnaire (HIVTSQ) is a 10-item self-reported scale that consists of a total score ranging from 0 to 60. Higher scores indicate a greater level of patient-reported satisfaction with their current therapy. ITT-E. Only those participants with data available at specified time points has been analyzed.

End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Week 24	

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	236	240		
Units: Scores on a scale				
arithmetic mean (standard deviation)	2.9 (± 5.85)	1 (± 5.16)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Participants who received DTG/3TC FDC v Participants who received CAR
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Adjusted Mean
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	2.2

Secondary: Change from Baseline in health status by HIV TSQ at Week 48

End point title	Change from Baseline in health status by HIV TSQ at Week 48
End point description:	
The HIVTSQ is a 10-item self-reported scale that consists of a total score ranging from 0 to 60. Higher scores indicate a greater level of patient-reported satisfaction with their current therapy. ITT-E. Only those participants with data available at specified time points has been analyzed.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Week 48	

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	229		
Units: Scores on a scale				
arithmetic mean (standard deviation)	2.9 (± 6)	1 (± 5.14)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Participants who received DTG/3TC FDC v Participants who received CAR
Number of subjects included in analysis	458
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Adjusted Mean
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	2.2

Secondary: Change from Baseline in health status by Symptom Distress Module (SDM) at Week 24

End point title	Change from Baseline in health status by Symptom Distress Module (SDM) at Week 24

End point description:

SDM is a 20-item self-reported measure that addresses the presence and perceived distress linked to symptoms commonly associated with HIV or its treatment. Each item is rated from 0 to 4 where 0 (complete absence of symptom) and 4 (very bothersome symptom). Overall score calculated as the sum of the scores for each of the 20 items of the questionnaire and ranged from 0 (best health) and 80 (worst health). ITT-E. Only those participants with data available at specified time points has been analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235	239		
Units: Scores on a scale				
arithmetic mean (standard deviation)	-2.6 (± 8.69)	-0.7 (± 8.01)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Participants who received DTG/3TC FDC v Participants who received CAR
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.021
Method	Mixed Model Repeated Measures
Parameter estimate	Adjusted Mean
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	-0.2

Secondary: Change from Baseline in health status by SDM at Week 48

End point title	Change from Baseline in health status by SDM at Week 48

End point description:

SDM is a 20-item self-reported measure that addresses the presence and perceived distress linked to symptoms commonly associated with HIV or its treatment. Each item is rated from 0 to 4 where 0 (complete absence of symptom) and 4 (very bothersome symptom). Overall score calculated as the sum of the scores for each of the 20 items of the questionnaire and ranged from 0 (best health) and 80 (worst health). ITT-E. Only those participants with data available at specified time points has been analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 48

End point values	Participants who received DTG/3TC FDC	Participants who received CAR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	228	226		
Units: Scores on a scale				
arithmetic mean (standard deviation)	-2.4 (± 7.64)	-1.5 (± 7.92)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Participants who received DTG/3TC FDC v Participants who received CAR
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.398
Method	Mixed Model Repeated Measures
Parameter estimate	Adjusted Mean
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	0.7

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All cause mortality, non-serious adverse events (Non-SAEs) and serious adverse events (SAEs) were collected from Day 1 to week 52.

Adverse event reporting additional description:

Safety Population included all randomized participants who received at least 1 dose of study intervention. The results presented are based on the primary analysis.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Participants who received DTG/3TC FDC

Reporting group description:

Eligible participants were randomized to receive 50 milligrams (mg)/300 mg DTG/3TC FDC therapy from day 1 up to 52 weeks. Participants who complete 52 weeks of treatment will have the opportunity to continue receiving DTG/3TC FDC once daily in the continuation phase.

Reporting group title	Participants who received CAR

Reporting group description:

Eligible participants received CAR from day 1 up to 52 weeks. CAR included 2 nucleoside reverse transcriptase inhibitors (NTRIs) plus either an integrase inhibitor (INI), non-nucleoside reverse transcriptase inhibitor (NNRTI), or boosted protease inhibitor (PI) or atazanavir unboosted

Serious adverse events	Participants who received DTG/3TC FDC	Participants who received CAR	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 246 (2.85%)	16 / 247 (6.48%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastrointestinal stromal tumour			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pituitary tumour benign			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the cervix			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Post procedural complication			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			

subjects affected / exposed	1 / 246 (0.41%)	3 / 247 (1.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Participants who received DTG/3TC FDC	Participants who received CAR	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	179 / 246 (72.76%)	169 / 247 (68.42%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign breast neoplasm			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Basal cell carcinoma			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Colon adenoma			

subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Dysplastic naevus			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Fibroadenoma of breast			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Hepatic neoplasm			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Lipoma			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Malignant melanoma			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	2	
Melanocytic naevus			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Seborrhoeic keratosis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Uterine leiomyoma			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 246 (2.44%)	7 / 247 (2.83%)	
occurrences (all)	7	7	
Hot flush			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	

Essential hypertension			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Peripheral coldness			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Peripheral venous disease			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Vasodilatation			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 246 (2.44%)	7 / 247 (2.83%)	
occurrences (all)	8	7	
Fatigue			
subjects affected / exposed	5 / 246 (2.03%)	6 / 247 (2.43%)	
occurrences (all)	5	6	
Chest pain			
subjects affected / exposed	1 / 246 (0.41%)	3 / 247 (1.21%)	
occurrences (all)	1	3	
Asthenia			
subjects affected / exposed	2 / 246 (0.81%)	1 / 247 (0.40%)	
occurrences (all)	2	1	
Chest discomfort			
subjects affected / exposed	2 / 246 (0.81%)	1 / 247 (0.40%)	
occurrences (all)	2	1	
Influenza like illness			
subjects affected / exposed	2 / 246 (0.81%)	1 / 247 (0.40%)	
occurrences (all)	2	1	
Feeling abnormal			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Pain			

subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Chills			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Cyst			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Ill-defined disorder			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Peripheral swelling			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	3	
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Hypersensitivity			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Seasonal allergy			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Social circumstances			
Stress at work			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			

Erectile dysfunction			
subjects affected / exposed	3 / 246 (1.22%)	1 / 247 (0.40%)	
occurrences (all)	3	1	
Vaginal haemorrhage			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Amenorrhoea			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Atrophic vulvovaginitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Dysmenorrhoea			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Menstruation delayed			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Pelvic pain			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Prostatitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Pruritus genital			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Uterine polyp			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Vaginal discharge			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	

Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	4 / 246 (1.63%)	2 / 247 (0.81%)	
occurrences (all)	4	2	
Cough			
subjects affected / exposed	3 / 246 (1.22%)	4 / 247 (1.62%)	
occurrences (all)	3	4	
Rhinitis allergic			
subjects affected / exposed	3 / 246 (1.22%)	1 / 247 (0.40%)	
occurrences (all)	4	1	
Respiratory disorder			
subjects affected / exposed	2 / 246 (0.81%)	1 / 247 (0.40%)	
occurrences (all)	2	1	
Dyspnoea			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Productive cough			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Asthma			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Dry throat			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Emphysema			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Hiccups			

subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Nasal discomfort			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Nasal dryness			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Nasal septum deviation			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Nasal obstruction			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Pharyngeal disorder			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Upper-airway cough syndrome			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	14 / 246 (5.69%)	4 / 247 (1.62%)	
occurrences (all)	15	4	
Anxiety			
subjects affected / exposed	5 / 246 (2.03%)	6 / 247 (2.43%)	
occurrences (all)	5	6	
Sleep disorder			
subjects affected / exposed	3 / 246 (1.22%)	3 / 247 (1.21%)	
occurrences (all)	3	3	

Depression			
subjects affected / exposed	2 / 246 (0.81%)	2 / 247 (0.81%)	
occurrences (all)	2	2	
Abnormal dreams			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Loss of libido			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Suicidal ideation			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Adjustment disorder			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Adjustment disorder with depressed mood			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Affective disorder			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Alcohol abuse			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Anxiety disorder			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Bipolar disorder			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Depressed mood			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Initial insomnia			

subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Mixed anxiety and depressive disorder			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Nightmare			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Stress			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Investigations			
Weight increased			
subjects affected / exposed	20 / 246 (8.13%)	5 / 247 (2.02%)	
occurrences (all)	20	5	
Low density lipoprotein increased			
subjects affected / exposed	2 / 246 (0.81%)	4 / 247 (1.62%)	
occurrences (all)	2	4	
Blood creatinine increased			
subjects affected / exposed	3 / 246 (1.22%)	3 / 247 (1.21%)	
occurrences (all)	3	3	
Blood cholesterol increased			
subjects affected / exposed	2 / 246 (0.81%)	3 / 247 (1.21%)	
occurrences (all)	2	3	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Blood glucose increased			

subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Blood pressure increased			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	2	
Blood triglycerides increased			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Creatinine renal clearance increased			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Glomerular filtration rate decreased			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Platelet count decreased			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Transaminases increased			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Urine protein/creatinine ratio increased			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Weight decreased			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Blood cholesterol decreased			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Blood creatine increased			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	

Blood glucose abnormal				
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)		
occurrences (all)	1	0		
Blood insulin increased				
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)		
occurrences (all)	0	1		
Blood prolactin increased				
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)		
occurrences (all)	0	1		
Blood urine present				
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)		
occurrences (all)	0	1		
Creatinine renal clearance decreased				
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)		
occurrences (all)	1	0		
Crystal urine present				
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)		
occurrences (all)	0	1		
Glucose urine present				
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)		
occurrences (all)	0	1		
Hepatic enzyme increased				
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)		
occurrences (all)	0	1		
Protein urine present				
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)		
occurrences (all)	0	1		
Pulse absent				
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)		
occurrences (all)	0	1		
SARS-CoV-2 test positive				
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)		
occurrences (all)	1	0		
Urine albumin/creatinine ratio increased				

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	2 / 246 (0.81%)	1 / 247 (0.40%)	
occurrences (all)	2	1	
Ankle fracture			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Muscle strain			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Vaccination complication			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Back injury			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Dental restoration failure			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Face injury			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Foot fracture			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Hand fracture			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Head injury			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Joint dislocation			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Joint injury			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Ligament sprain			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Limb injury			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Neck injury			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Pelvic organ injury			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Penis injury			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Post procedural complication			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Post-traumatic pain			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Road traffic accident			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Skin abrasion			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Skin injury			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Spinal compression fracture			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Upper limb fracture			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Congenital, familial and genetic disorders			
Dysplastic naevus syndrome			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Left ventricular hypertrophy			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Myocardial ischaemia			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	13 / 246 (5.28%)	6 / 247 (2.43%)	
occurrences (all)	15	7	
Headache			
subjects affected / exposed	16 / 246 (6.50%)	17 / 247 (6.88%)	
occurrences (all)	18	20	
Hypoaesthesia			
subjects affected / exposed	1 / 246 (0.41%)	2 / 247 (0.81%)	
occurrences (all)	2	2	
Paraesthesia			
subjects affected / exposed	1 / 246 (0.41%)	2 / 247 (0.81%)	
occurrences (all)	1	2	
Sciatica			

subjects affected / exposed	0 / 246 (0.00%)	3 / 247 (1.21%)	
occurrences (all)	0	3	
Memory impairment			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Presyncope			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Sensory loss			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Syncope			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Ageusia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Anosmia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Burning sensation			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Cervical radiculopathy			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Cervicobrachial syndrome			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Dysgeusia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Hemianopia heteronymous			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Hemiparesis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Nerve compression			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Neuralgia			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 246 (0.81%)	5 / 247 (2.02%)	
occurrences (all)	2	6	
Lymphadenopathy			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Neutropenia			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	3 / 246 (1.22%)	0 / 247 (0.00%)	
occurrences (all)	3	0	
Ear pain			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Cerumen impaction			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Ear discomfort			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Ear pruritus			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Hypoacusis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Meniere's disease			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Tinnitus			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Cataract			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Conjunctival haemorrhage			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Conjunctivitis allergic			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Glaucoma			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Ocular hypertension			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	

Vision blurred			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	2	
Visual acuity reduced			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	4 / 246 (1.63%)	5 / 247 (2.02%)	
occurrences (all)	4	7	
Constipation			
subjects affected / exposed	1 / 246 (0.41%)	6 / 247 (2.43%)	
occurrences (all)	1	6	
Nausea			
subjects affected / exposed	6 / 246 (2.44%)	4 / 247 (1.62%)	
occurrences (all)	7	6	
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 246 (1.63%)	7 / 247 (2.83%)	
occurrences (all)	4	7	
Diarrhoea			
subjects affected / exposed	7 / 246 (2.85%)	8 / 247 (3.24%)	
occurrences (all)	7	9	
Abdominal pain			
subjects affected / exposed	4 / 246 (1.63%)	1 / 247 (0.40%)	
occurrences (all)	5	1	
Dyspepsia			
subjects affected / exposed	4 / 246 (1.63%)	1 / 247 (0.40%)	
occurrences (all)	4	1	
Abdominal pain upper			
subjects affected / exposed	3 / 246 (1.22%)	2 / 247 (0.81%)	
occurrences (all)	3	3	
Flatulence			
subjects affected / exposed	3 / 246 (1.22%)	2 / 247 (0.81%)	
occurrences (all)	3	2	
Toothache			

subjects affected / exposed	3 / 246 (1.22%)	2 / 247 (0.81%)	
occurrences (all)	3	2	
Vomiting			
subjects affected / exposed	3 / 246 (1.22%)	2 / 247 (0.81%)	
occurrences (all)	3	2	
Abdominal pain lower			
subjects affected / exposed	2 / 246 (0.81%)	2 / 247 (0.81%)	
occurrences (all)	2	2	
Gastritis			
subjects affected / exposed	1 / 246 (0.41%)	3 / 247 (1.21%)	
occurrences (all)	1	3	
Dental caries			
subjects affected / exposed	3 / 246 (1.22%)	0 / 247 (0.00%)	
occurrences (all)	3	0	
Umbilical hernia			
subjects affected / exposed	1 / 246 (0.41%)	2 / 247 (0.81%)	
occurrences (all)	1	2	
Haemorrhoids			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Abdominal discomfort			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Anogenital dysplasia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Anal fissure			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Colitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Colitis ulcerative			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Diverticulum intestinal			

subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Duodenitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Dysphagia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Food poisoning			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Frequent bowel movements			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Gastric cyst			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Gastric dilatation			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorder			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Gingival pain			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Gingival swelling			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Hiatus hernia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Inguinal hernia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Irritable bowel syndrome			

subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Lip swelling			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	6 / 246 (2.44%)	1 / 247 (0.40%)	
occurrences (all)	7	1	
Dermatitis			
subjects affected / exposed	4 / 246 (1.63%)	1 / 247 (0.40%)	
occurrences (all)	5	1	
Acne			
subjects affected / exposed	3 / 246 (1.22%)	2 / 247 (0.81%)	
occurrences (all)	3	2	
Eczema			
subjects affected / exposed	1 / 246 (0.41%)	2 / 247 (0.81%)	
occurrences (all)	1	3	
Alopecia			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Dermal cyst			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Dermatitis allergic			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Dry skin			

subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Pruritus			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Rash papular			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Skin lesion			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Actinic keratosis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Dermatitis atopic			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Dermatitis bullous			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Dyshidrotic eczema			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Lichen planus			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Miliaria			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Night sweats			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Photosensitivity reaction			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Pseudofolliculitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Psoriasis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Rash maculo-papular			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Rash erythematous			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Rosacea			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Skin odour abnormal			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Skin ulcer			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Skin plaque			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Solar dermatitis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Solar lentigo			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	4 / 246 (1.63%)	3 / 247 (1.21%)	
occurrences (all)	4	3	
Haematuria			
subjects affected / exposed	1 / 246 (0.41%)	2 / 247 (0.81%)	
occurrences (all)	1	2	
Proteinuria			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Acute kidney injury			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Dysuria			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Glycosuria			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Nephrolithiasis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Renal colic			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Urinary incontinence			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Urine odour abnormal			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Acromegaly			

subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Diabetes insipidus			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Hypopituitarism			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Secondary adrenocortical insufficiency			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Secondary hypothyroidism			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Thyroid disorder			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 246 (2.03%)	10 / 247 (4.05%)	
occurrences (all)	5	11	
Back pain			
subjects affected / exposed	14 / 246 (5.69%)	7 / 247 (2.83%)	
occurrences (all)	15	7	
Myalgia			
subjects affected / exposed	5 / 246 (2.03%)	1 / 247 (0.40%)	
occurrences (all)	5	1	
Pain in extremity			
subjects affected / exposed	5 / 246 (2.03%)	3 / 247 (1.21%)	
occurrences (all)	5	3	
Neck pain			
subjects affected / exposed	4 / 246 (1.63%)	4 / 247 (1.62%)	
occurrences (all)	4	6	
Muscle spasms			

subjects affected / exposed	2 / 246 (0.81%)	2 / 247 (0.81%)	
occurrences (all)	3	2	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Rotator cuff syndrome			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Spinal osteoarthritis			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	2	
Bone formation increased			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Cervical spinal stenosis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Chondropathy			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Finger deformity			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Jaw cyst			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Joint effusion			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Muscle fatigue			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Muscle tightness			

subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Muscular weakness			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Musculoskeletal discomfort			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Osteoarthritis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Patellofemoral pain syndrome			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Rhabdomyolysis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Tendon pain			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	14 / 246 (5.69%)	8 / 247 (3.24%)	
occurrences (all)	14	8	
Gastroenteritis			
subjects affected / exposed	3 / 246 (1.22%)	5 / 247 (2.02%)	
occurrences (all)	3	5	
Nasopharyngitis			
subjects affected / exposed	11 / 246 (4.47%)	9 / 247 (3.64%)	
occurrences (all)	12	10	

Syphilis			
subjects affected / exposed	9 / 246 (3.66%)	5 / 247 (2.02%)	
occurrences (all)	10	5	
Urinary tract infection			
subjects affected / exposed	3 / 246 (1.22%)	5 / 247 (2.02%)	
occurrences (all)	4	5	
Upper respiratory tract infection			
subjects affected / exposed	11 / 246 (4.47%)	15 / 247 (6.07%)	
occurrences (all)	11	16	
Sinusitis			
subjects affected / exposed	1 / 246 (0.41%)	4 / 247 (1.62%)	
occurrences (all)	1	4	
Conjunctivitis			
subjects affected / exposed	2 / 246 (0.81%)	3 / 247 (1.21%)	
occurrences (all)	2	3	
Bronchitis			
subjects affected / exposed	2 / 246 (0.81%)	2 / 247 (0.81%)	
occurrences (all)	2	2	
Chlamydial infection			
subjects affected / exposed	2 / 246 (0.81%)	2 / 247 (0.81%)	
occurrences (all)	2	3	
Influenza			
subjects affected / exposed	1 / 246 (0.41%)	3 / 247 (1.21%)	
occurrences (all)	1	3	
Onychomycosis			
subjects affected / exposed	2 / 246 (0.81%)	2 / 247 (0.81%)	
occurrences (all)	2	2	
Otitis externa			
subjects affected / exposed	1 / 246 (0.41%)	3 / 247 (1.21%)	
occurrences (all)	1	3	
Pharyngitis			
subjects affected / exposed	2 / 246 (0.81%)	2 / 247 (0.81%)	
occurrences (all)	2	2	
Proctitis gonococcal			
subjects affected / exposed	1 / 246 (0.41%)	3 / 247 (1.21%)	
occurrences (all)	1	3	

Herpes zoster			
subjects affected / exposed	2 / 246 (0.81%)	1 / 247 (0.40%)	
occurrences (all)	2	2	
Oropharyngeal gonococcal infection			
subjects affected / exposed	2 / 246 (0.81%)	1 / 247 (0.40%)	
occurrences (all)	2	1	
Respiratory tract infection			
subjects affected / exposed	2 / 246 (0.81%)	1 / 247 (0.40%)	
occurrences (all)	2	1	
Rhinitis			
subjects affected / exposed	2 / 246 (0.81%)	1 / 247 (0.40%)	
occurrences (all)	2	1	
Suspected COVID-19			
subjects affected / exposed	1 / 246 (0.41%)	2 / 247 (0.81%)	
occurrences (all)	1	2	
Cellulitis			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Cystitis			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Ear infection			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Furuncle			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Fungal skin infection			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	2	
Gastrointestinal infection			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Gonococcal infection			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	2	1	

Gonorrhoea			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Herpes simplex			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	2	1	
Lower respiratory tract infection			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Oral herpes			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	3	0	
Pharyngotonsillitis			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Periodontitis			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Primary syphilis			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Subcutaneous abscess			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Tonsillitis			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Viral infection			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Acarodermatitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Anal chlamydia infection			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	

Anorectal human papilloma virus infection				
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)		
occurrences (all)	0	1		
Bacterial vaginosis				
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)		
occurrences (all)	1	0		
Body tinea				
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)		
occurrences (all)	1	0		
Bronchitis viral				
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)		
occurrences (all)	1	0		
Candida infection				
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)		
occurrences (all)	1	0		
Chronic sinusitis				
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)		
occurrences (all)	0	1		
Conjunctivitis bacterial				
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)		
occurrences (all)	1	0		
Eyelid infection				
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)		
occurrences (all)	1	0		
Folliculitis				
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)		
occurrences (all)	1	0		
Fungal infection				
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)		
occurrences (all)	0	1		
Gastroenteritis viral				
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)		
occurrences (all)	0	2		
Genital herpes				

subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Genital herpes simplex			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Genitourinary chlamydia infection			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Laryngitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Localised infection			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Otitis media acute			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Paronychia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Pharyngeal chlamydia infection			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Pneumonia bacterial			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Pneumonia viral			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Secondary syphilis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Sinusitis bacterial			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Skin infection			

subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Tinea capitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Tinea infection			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	2	
Tinea pedis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Tooth infection			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Tracheitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Urethritis			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Urethritis gonococcal			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	1 / 246 (0.41%)	5 / 247 (2.02%)	
occurrences (all)	1	5	
Hyperlipidaemia			
subjects affected / exposed	4 / 246 (1.63%)	1 / 247 (0.40%)	
occurrences (all)	4	1	
Dyslipidaemia			
subjects affected / exposed	0 / 246 (0.00%)	4 / 247 (1.62%)	
occurrences (all)	0	4	

Hypercholesterolaemia			
subjects affected / exposed	3 / 246 (1.22%)	3 / 247 (1.21%)	
occurrences (all)	3	3	
Hyperglycaemia			
subjects affected / exposed	2 / 246 (0.81%)	3 / 247 (1.21%)	
occurrences (all)	2	3	
Decreased appetite			
subjects affected / exposed	3 / 246 (1.22%)	0 / 247 (0.00%)	
occurrences (all)	3	0	
Glucose tolerance impaired			
subjects affected / exposed	1 / 246 (0.41%)	2 / 247 (0.81%)	
occurrences (all)	1	2	
Insulin resistance			
subjects affected / exposed	0 / 246 (0.00%)	3 / 247 (1.21%)	
occurrences (all)	0	3	
Vitamin D deficiency			
subjects affected / exposed	1 / 246 (0.41%)	2 / 247 (0.81%)	
occurrences (all)	1	2	
Abnormal loss of weight			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Diabetes mellitus			
subjects affected / exposed	1 / 246 (0.41%)	1 / 247 (0.40%)	
occurrences (all)	1	1	
Hypokalaemia			
subjects affected / exposed	0 / 246 (0.00%)	2 / 247 (0.81%)	
occurrences (all)	0	2	
Increased appetite			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Metabolic syndrome			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	
Type 2 diabetes mellitus			
subjects affected / exposed	2 / 246 (0.81%)	0 / 247 (0.00%)	
occurrences (all)	2	0	

Dehydration			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Hyperuricaemia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Hypoglycaemia			
subjects affected / exposed	0 / 246 (0.00%)	1 / 247 (0.40%)	
occurrences (all)	0	1	
Obesity			
subjects affected / exposed	1 / 246 (0.41%)	0 / 247 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 March 2018	A global amendment applicable to all participating countries to clarify entry criteria, correct errors and improve consistency.
14 November 2018	A global amendment applicable to all participating countries to update the study design including length of study, updates to the eligibility criteria and removing the option to remain on the study if the participant becomes pregnant. Additional changes were made to manage and mitigate risks following identification of a potential safety issue related to neural tube defects in infants born to women with exposure to dolutegravir at the time of conception. A sub-study was added to collect data on participants who withdraw for meeting CVW or PVW criteria.
25 March 2019	A global amendment, for administrative purposes, applicable to all participating countries. Edits to increase clarity around collection of virology specimens for additional testing, the timing of the eCSSRS questionnaire in relation to medication administration, and follow-up for AEs were made. Additional changes were made to correct editing errors related to the tables for liver stopping criteria, which contained both GSK and ViiV-specific stopping criteria. This amendment removed the GSK information.
05 May 2020	This global amendment describes possible changes in patient management related to the impact of COVID-19, COVID-19 case definition guidance, ending recruitment due to COVID-19 before the original sample size was achieved and sample size considerations and statistical analyses updates. Additionally, the list of prohibited medications was updated to add fampridine to align with the Investigator Brochure version 13 and other administrative updates were made to provide updated information, correct errors and improve accuracy and consistency.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/35235656