Clinical trial results:
An open-label, multi-centre, randomised, switch study to evaluate the virological efficacy over 96 weeks of 2-drug therapy with DTG+RPV FDC in antiretroviral treatment-experienced HIV-1 infected subjects virologically suppressed with NNRTIs resistance mutation K103N.

Summary

EudraCT number	2017-004040-38
Trial protocol	GB FR DE BE ES IT
Global end of trial date	09 November 2022

Results information

Result version number	v1 (current)
This version publication date	20 July 2024
First version publication date	20 July 2024

Trial information

Trial identification

Sponsor protocol code	SSCR105/NEAT33

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05349838
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	NEAT ID Foundation
Sponsor organisation address	56 Rue des Colonies, Brussels, Belgium, 1000 Brussels
Public contact	WISARD Clinical Project Manager, Research Organisation KC, 0044 7376618244, WISARD@rokcservices.com
Scientific contact	Graeme Moyle, Chelsea and Westminster Hospital, 0044 020 7938 2355, geyyom@gmail.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 November 2022
Global end of trial reached?	Yes
Global end of trial date	09 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare efficacy of DTG/RPV combined tablet versus continued antiretroviral treatment regimen at 48 weeks in individuals with the K103N resistance mutation.

Protection of trial subjects:

Insurance was put in place to protect trial subjects.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	15 October 2018
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	Spain: 22
Country: Number of subjects enrolled	United Kingdom: 52
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	France: 36
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Italy: 10
Worldwide total number of subjects	140
EEA total number of subjects	88

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	125
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment began with first subject consented on 15-Oct-2018 and ended with last final subject enrolled on 10-Dec-2020. Subjects were recruited from sites in the following territories: UK, Spain, France, Belgium, Italy, Germany, Ireland.

Pre-assignment

Screening details:

All subjects selected as potential suitable for the study were screened within a 30 days of the baseline visit. The purpose of the screening visits was to assess subjects for eligibility based on the eligibility criteria in the protocol. Screening data was entered into the eCRF by the study site staff and assessed by staff at the CRO.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A - Immediate switch

Arm description:

Participants randomised to this arm switch to Dolutegravir/Rilpivirine Fixed Dose Combination (Juluca) at baseline.

Arm type	Experimental
Investigational medicinal product name	Juluca (Dolutegravir and Rilpivirine Fixed Dose Combination)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One combined Dolutegravir 50mg/Rilpivirine 25mg Fixed Dose Combination tablet taken orally once daily for 96 weeks.

Arm title	Arm B - Deferred switch

Arm description:

Subjects randomised to this arm continued on their current antiretroviral treatment until week 48 and then switched to the study IMP. They remained on the study IMP until week 96.

Arm type	Active comparator
Investigational medicinal product name	Juluca (Dolutegravir and Rilpivirine Fixed Dose Combination)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One combined Dolutegravir 50mg/Rilpivirine 25mg Fixed Dose Combination tablet taken orally once daily from week 48 to week 96.

Number of subjects in period 1	Arm A - Immediate switch	Arm B - Deferred switch
Started	95	45
Completed	83	37
Not completed	12	8
Consent withdrawn by subject	2	3
Physician decision	1	1
Adverse event, non-fatal	3	1
Virological Failure	1	2
Patient relocation to another country	2	-
Lost to follow-up	1	1
Concomitant Medication	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm A - Immediate switch
Reporting group description:	
Participants randomised to this arm switch to Dolutegravir/Rilpivirine Fixed Dose Combination (Juluca) at baseline.	
Reporting group title	Arm B - Deferred switch
Reporting group description:	
Subjects randomised to this arm continued on their current antiretroviral treatment until week 48 and then switched to the study IMP. They remained on the study IMP until week 96.	

Reporting group values	Arm A - Immediate switch	Arm B - Deferred switch	Total
Number of subjects	95	45	140
Age categorical			
Units: Subjects			
Adults (18-64 years)	84	42	126
From 65-84 years	11	3	14
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	16	10	26
Male	79	35	114
Ethnicity			
subject ethnicity at baseline			
Units: Subjects			
White caucasian	69	29	98
White mixed	2	1	3
Asian	4	0	4
Black	7	7	14
African	3	3	6
Caribbean	1	1	2
Other	9	4	13
Time since HIV diagnosis (years)			
Time since HIV diagnosis (years)			
Units: Years			
median	17.1	22.4	
inter-quartile range (Q1-Q3)	7.3 to 26.3	13.1 to 26.5	-
Duration of Antiretroviral Treatment (ART) (years)			
Duration of Antiretroviral Treatment (ART) (years)			
Units: Years			
median	16	17.7	
inter-quartile range (Q1-Q3)	6.3 to 23	10.5 to 23	-

Subject analysis sets	
Subject analysis set title	All subjects
Subject analysis set type	Full analysis

Subject analysis set description:
Analysis on Arm A Immediate switch and Arm B Deferred switch

Reporting group values	All subjects		
Number of subjects	140		
Age categorical Units: Subjects			
Adults (18-64 years)	126		
From 65-84 years	14		
85 years and over	0		
Gender categorical Units: Subjects			
Female	26		
Male	114		
Ethnicity			
subject ethnicity at baseline			
Units: Subjects			
White caucasian	98		
White mixed	3		
Asian	4		
Black	14		
African	6		
Caribbean	2		
Other	13		
Time since HIV diagnosis (years)			
Time since HIV diagnosis (years)			
Units: Years			
median	19.7		
inter-quartile range (Q1-Q3)	8.8 to 26.4		
Duration of Antiretroviral Treatment (ART) (years)			
Duration of Antiretroviral Treatment (ART) (years)			
Units: Years			
median	16.5		
inter-quartile range (Q1-Q3)	7.3 to 23		

End points

End points reporting groups

Reporting group title	Arm A - Immediate switch

Reporting group description:

Participants randomised to this arm switch to Dolutegravir/Rilpivirine Fixed Dose Combination (Juluca) at baseline.

Reporting group title	Arm B - Deferred switch

Reporting group description:

Subjects randomised to this arm continued on their current antiretroviral treatment until week 48 and then switched to the study IMP. They remained on the study IMP until week 96.

Subject analysis set title	All subjects
Subject analysis set type	Full analysis

Subject analysis set description:

Analysis on Arm A Immediate switch and Arm B Deferred switch

Primary: Virological Response at Week 48

End point title	Virological Response at Week 48

End point description:

End point type	Primary

End point timeframe:

Week 48

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	45		
Units: Percentage				
number (confidence interval 95%)				
HIV RNA <50 copies/mL	88.4 (80.2 to 94.1)	88.9 (75.9 to 96.3)		
HIV RNA >=50 copies/mL	3.2 (0.7 to 9.0)	2.2 (0.1 to 11.8)		
No virologic data at week 48	8.4 (3.7 to 15.9)	8.9 (2.5 to 21.2)		

Attachments (see zip file)	FDA Snapshot Week 48.png

Statistical analyses

Statistical analysis title	ITT FDA Snapshot

Statistical analysis description:

Proportion of participants with HIV-RNA <50 copies/mL at week 48,
with the ITT FDA Snapshot method

Comparison groups	Arm A - Immediate switch v Arm B - Deferred switch

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.1
Method	Regression, Logistic
Parameter estimate	ITT FDA Snapshot
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Notes:

[1] - The two-sided 95% confidence interval of the difference in therapeutic success rate will be calculated.
The effect of study treatment will also be assessed in the mITT population using logistic regression model with treatment group adjusted for the presence of M184V mutation at baseline and CD4 count at baseline (above versus below 350 cells/µL) as well as all baseline variables potentially associated with the outcome, with univariable P-value <0.10.

Secondary: Change from baseline in CD4 cell count

End point title	Change from baseline in CD4 cell count

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48, Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	45		
Units: count/mm3				
arithmetic mean (standard error)				
Change from baseline to week 48	-31.7 (± 34.8)	9.2 (± 51)		
Change from week 48 to week 96	27.3 (± 36.3)	-9.8 (± 55.3)		
Change from baseline to week 96	-4.4 (± 47.1)	-0.7 (± 71.0)		

Attachments (see zip file)	Change from BL in CD4 cell count.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in CD8 cell count

End point title	Change from baseline in CD8 cell count

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	45		
Units: count/mm3				
arithmetic mean (standard error)				
Change from baseline to week 48	-58.8 (± 41.3)	9.7 (± 60.4)		
Change from week 48 to week 96	-5.7 (± 43.2)	-55.8 (± 66.6)		
Change from baseline to week 96	-64.5 (± 53.4)	-46.1 (± 81.3)		

Attachments (see zip file)	Change from BL in CD8 cell count.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in CD4/CD8 ratio

End point title	Change from baseline in CD4/CD8 ratio

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	45		
Units: Cd4/Cd8 ratio				
arithmetic mean (standard error)				
Change from baseline to week 48	0.03 (± 0.06)	0.02 (± 0.09)		
Change from week 48 to week 96	0.04 (± 0.06)	0 (± 0.10)		
Change from baseline to week 96	0.07 (± 0.08)	0.01 (± 0.13)		

Attachments (see zip file)	Change from BL in CD4 CD8 ratio.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in body weight

End point title	Change from baseline in body weight

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	45		
Units: Body weight, kg				
arithmetic mean (standard error)				
Change from baseline to week 48	0.7 (± 2.1)	1.3 (± 3.1)		
Change from week 48 to week 96	1.7 (± 2.2)	1.3 (± 3.4)		
Change from baseline to week 96	2.4 (± 3.0)	2.6 (± 4.5)		

Attachments (see zip file)	Change from BL in body weight.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in BMI

End point title	Change from baseline in BMI

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	45		
Units: kg/m2				
arithmetic mean (standard error)				
Change from baseline to week 48	0.3 (± 0.6)	0.6 (± 0.9)		
Change from week 48 to week 96	0.5 (± 0.7)	0.3 (± 1.0)		
Change from baseline to week 96	0.8 (± 0.9)	0.9 (± 1.3)		

Attachments (see zip file)	Change from BL in BMI.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in hsCRP

End point title	Change from baseline in hsCRP

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	24		
Units: mg/L				
arithmetic mean (standard error)				
Change from baseline to week 48	0.8 (± 1.2)	-1.3 (± 1.8)		
Change from week 48 to week 96	0.5 (± 1.2)	-0.9 (± 1.9)		
Change from baseline to week 96	1.3 (± 1.4)	-2.2 (± 2.1)		

Attachments (see zip file)	Change from BL in hsCRP.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Systolic Blood Pressure

End point title	Change from baseline in Systolic Blood Pressure

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	45		
Units: mmHg				
arithmetic mean (standard error)				
Change from baseline to week 48	-1.4 (± 2.2)	4.9 (± 3.3)		
Change from week 48 to week 96	-0.1 (± 2.3)	5.6 (± 3.6)		
Change from baseline to week 96	-1.5 (± 2.7)	10.5 (± 4.1)		

Attachments (see zip file)	Change from BL in systolic blood pressure.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Diastolic Blood Pressure

End point title	Change from baseline in Diastolic Blood Pressure

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	45		
Units: mmHg				
arithmetic mean (standard error)				
Change from baseline to week 48	0.2 (± 1.5)	3.1 (± 2.2)		
Change from week 48 to week 96	-0.7 (± 1.6)	0.8 (± 2.4)		
Change from baseline to week 96	-0.5 (± 1.8)	4.0 (± 2.7)		

Attachments (see zip file)	Change from BL in diastolic blood pressure.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Pulse rate

End point title	Change from baseline in Pulse rate

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	45		
Units: Pulse rate				
arithmetic mean (standard error)				
Change from baseline to week 48	2.1 (± 1.6)	2.7 (± 2.4)		
Change from week 48 to week 96	-2.5 (± 1.8)	-1.5 (± 2.6)		
Change from baseline to week 96	-0.4 (± 2.0)	1.2 (± 2.9)		

Attachments (see zip file)	Change from BL in pulse.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Red blood cells

End point title	Change from baseline in Red blood cells

End point description:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	45		
Units: 10^12/L				
arithmetic mean (standard error)				
Change from baseline to week 48	0.20 (± 0.06)	-0.07 (± 0.09)		
Change from week 48 to week 96;	-0.02 (± 0.07)	0.19 (± 0.10)		
Change from baseline to week 96	0.17 (± 0.09)	0.12 (± 0.13)		

Attachments (see zip file)	Change from BL in RBC.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in White blood cells

End point title	Change from baseline in White blood cells

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	45		
Units: 10^12/L				
arithmetic mean (standard error)				
Change from baseline to week 48	-0.08 (± 0.26)	-0.06 (± 0.38)		
Change from week 48 to week 96	0.09 (± 0.27)	-0.03 (± 0.41)		
Change from baseline to week 96	0.01 (± 0.34)	-0.09 (± 0.51)		

Attachments (see zip file)	Change from BL in WBC.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Platelet counts

End point title	Change from baseline in Platelet counts

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	45		
Units: 10^9/L				
arithmetic mean (standard error)				
Change from baseline to week 48	3.4 (± 8.2)	-2.6 (± 12.1)		
Change from week 48 to week 96	0.6 (± 8.6)	9.3 (± 13.1)		
Change from baseline to week 96	4.0 (± 11.1)	6.7 (± 16.8)		

Attachments (see zip file)	Change from BL in Platelet count.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Haemoglobin

End point title	Change from baseline in Haemoglobin

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	45		
Units: g/dL				
arithmetic mean (standard error)				
Change from baseline to week 48	0.1 (± 0.2)	0 (± 0.3)		
Change from week 48 to week 96	0 (± 0.2)	0.2 (± 0.3)		
Change from baseline to week 96	0.1 (± 0.3)	0.2 (± 0.4)		

Attachments (see zip file)	Change from BL in haemoglobin.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Sodium

End point title	Change from baseline in Sodium

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	45		
Units: mmol/L				
arithmetic mean (standard error)				
Change from baseline to week 48	0.3 (± 0.3)	-0.8 (± 0.4)		
Change from week 48 to week 96	-0.5 (± 0.3)	0.3 (± 0.4)		
Change from baseline to week 96	-0.2 (± 0.3)	-0.5 (± 0.5)		

Attachments (see zip file)	Change from BL in sodium.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in ALT

End point title	Change from baseline in ALT

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	45		
Units: U/L				
arithmetic mean (standard error)				
Change from baseline to week 48	2.4 (± 3.2)	-0.6 (± 4.7)		
Change from week 48 to week 96	-0.7 (± 3.4)	1.1 (± 5.1)		
Change from baseline to week 96	1.8 (± 3.7)	0.6 (± 5.6)		

Attachments (see zip file)	Change from BL in ALT.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Total Bilirubin

End point title	Change from baseline in Total Bilirubin

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	45		
Units: umol/L				
arithmetic mean (standard error)				
Change from baseline to week 48	-0.6 (± 1.4)	-1.9 (± 2.0)		
Change from week 48 to week 96	-1.3 (± 1.4)	-2.2 (± 2.2)		
Change from baseline to week 96	-1.9 (± 1.4)	-4.1 (± 2.1)		

Attachments (see zip file)	Change from BL in bilirubin.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Glucose

End point title	Change from baseline in Glucose

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	43		
Units: mmol/L				
arithmetic mean (standard error)				
Change from baseline to week 48	-0.15 (± 0.16)	-0.06 (± 0.23)		
Change from week 48 to week 96	0.09 (± 0.17)	-0.11 (± 0.25)		
Change from baseline to week 96	-0.06 (± 0.21)	-0.17 (± 0.31)		

Attachments (see zip file)	Change from BL in glucose.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Total Cholesterol

End point title	Change from baseline in Total Cholesterol

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	45		
Units: mmol/L				
arithmetic mean (standard error)				
Change from baseline to week 48	-0.09 (± 0.14)	0.05 (± 0.20)		
Change from week 48 to week 96	0.02 (± 0.15)	-0.19 (± 0.22)		
Change from baseline to week 96	-0.07 (± 0.18)	-0.13 (± 0.27)		

Attachments (see zip file)	Change from BL in total cholesterol.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in HDL cholesterol

End point title	Change from baseline in HDL cholesterol

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	44		
Units: mmol/L				
arithmetic mean (standard error)				
Change from baseline to week 48	0.06 (± 0.05)	0.03 (± 0.07)		
Change from week 48 to week 96	-0.03 (± 0.05)	0.01 (± 0.08)		
Change from baseline to week 96	0.03 (± 0.06)	0.04 (± 0.10)		

Attachments (see zip file)	Change from BL in HDL cholesterol.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in LDL cholesterol

End point title	Change from baseline in LDL cholesterol

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	42		
Units: mmol/L				
arithmetic mean (standard error)				
Change from baseline to week 48	-0.05 (± 0.12)	0 (± 0.18)		
Change from week 48 to week 96	0.02 (± 0.12)	-0.14 (± 0.19)		
Change from baseline to week 96	-0.02 (± 0.15)	-0.14 (± 0.23)		

Attachments (see zip file)	Change from BL in LDL cholesterol.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Triglycerides

End point title	Change from baseline in Triglycerides

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	45		
Units: mmol/L				
arithmetic mean (standard error)				
Change from baseline to week 48	-0.26 (± 0.15)	-0.02 (± 0.22)		
Change from week 48 to week 96	0.14 (± 0.15)	-0.16 (± 0.23)		
Change from baseline to week 96	-0.12 (± 0.18)	-0.18 (± 0.27)		

Attachments (see zip file)	Change from BL in triglycerides.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Creatinine

End point title	Change from baseline in Creatinine

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	44		
Units: umol/L				
arithmetic mean (standard error)				
Change from baseline to week 48	3.0 (± 2.3)	0.3 (± 3.4)		
Change from week 48 to week 9	0.3 (± 2.4)	5.5 (± 3.7)		
Change from baseline to week 96	3.3 (± 3.1)	5.8 (± 4.7)		

Attachments (see zip file)	Change from BL in creatinine.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Creatinine clearance

End point title	Change from baseline in Creatinine clearance

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	44		
Units: mL/min				
arithmetic mean (standard error)				
Change from baseline to week 48	-1.7 (± 2.2)	-1.3 (± 3.3)		
Change from week 48 to week 96	-1.2 (± 2.3)	-3.4 (± 3.6)		
Change from baseline to week 96	-2.9 (± 2.8)	-4.7 (± 4.2)		

Attachments (see zip file)	Change from BL in creatinine clearance.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in ALP

End point title	Change from baseline in ALP

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	45		
Units: U/L				
arithmetic mean (standard error)				
Change from baseline to week 48	-5.3 (± 3.0)	-1.5 (± 4.3)		
Change from week 48 to week 96	3.1 (± 3.1)	-2.5 (± 4.7)		
Change from baseline to week 96	-2.2 (± 4.0)	-4.0 (± 6.0)		

Attachments (see zip file)	Change from BL in ALP.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in QOL Health status score

End point title	Change from baseline in QOL Health status score

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	43		
Units: Health status score				
arithmetic mean (standard error)				
Change from baseline to week 48	1.7 (± 2.9)	6.3 (± 4.3)		
Change from week 48 to week 96	-2.0 (± 3.0)	-7.2 (± 4.6)		
Change from baseline to week 96	-0.3 (± 3.3)	-0.9 (± 5.0)		

Attachments (see zip file)	Change from BL in QoL Health score.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in patients' satisfaction

End point title	Change from baseline in patients' satisfaction

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	45		
Units: Global satisfaction score				
arithmetic mean (standard error)				
Change from baseline to week 48	1.6 (± 0.6)	0.7 (± 0.9)		
Change from week 48 to week 96	0.2 (± 0.6)	0.4 (± 1.0)		
Change from baseline to week 96	1.8 (± 0.7)	1.1 (± 1.1)		

Attachments (see zip file)	Change from BL in patient satisfaction.png

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Global Pittsburgh Sleep Quality Index (PSQI) score

End point title	Change from baseline in Global Pittsburgh Sleep Quality Index (PSQI) score

End point description:

End point type	Secondary

End point timeframe:

Change from baseline to week 48; Change from week 48 to week 96; Change from baseline to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	40		
Units: Global PSQI Score				
arithmetic mean (standard error)				
Change from baseline to week 48	-0.1 (± 0.3)	-0.7 (± 0.5)		
Change from week 48 to week 96	0 (± 0.3)	-0.5 (± 0.5)		
Change from baseline to week 96	-0.1 (± 0.3)	-1.2 (± 0.5)		

Attachments (see zip file)	Change from BL in PSQI.png

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events (AEs) from baseline to week 48

End point title	Number of participants with adverse events (AEs) from baseline to week 48

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 48

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	45		
Units: Number				
number (not applicable)				
Any AEs	78	33		
Grade 1	61	25		
Grade 2	43	13		

Grade 3-4	7	2		
Drug related AEs	22	0		
Drug related grade 3-4 AEs	1	0		
AE leading to the study drugs interruption	4	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events (AEs) Week 48 to week 96

End point title	Number of participants with adverse events (AEs) Week 48 to week 96

End point description:

End point type	Secondary

End point timeframe:

Week 48 to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	34		
Units: Number				
number (not applicable)				
Any AEs	54	28		
Grade 1	36	18		
Grade 2	20	12		
Grade 3-4	5	5		
Drug related AEs	1	5		
Drug related grade 3-4 AEs	0	0		
AEs leading to the study drugs interruption	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of drug-drug interactions

End point title	Number of drug-drug interactions[2]

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 96

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Both arms reported separately due to different timepoints reported.

End point values	Arm A - Immediate switch			
Subject group type	Reporting group			
Number of subjects analysed	95			
Units: Number				
Baseline	90			
Week 24	88			
Week 48	86			
Week 96	81			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Adverse Events (AEs) from baseline to week 48

End point title	Number of participants with Adverse Events (AEs) from baseline to week 48

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 48

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	45		
Units: number				
Any AEs	78	33		
Grade 1	61	25		
Grade 2	43	13		
Grade 3-4	7	2		
Drug related AEs	22	0		
Drug related grade 3-4 AEs	1	0		
AEs leading to the study drug interruption	4	0		
Missing Grade	6	1		
Serious Adverse Events (SAEs)	4	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events (AEs) from week 48 to week 96

End point title	Number of participants with adverse events (AEs) from week 48 to week 96

End point description:

End point type	Secondary

End point timeframe:

week 48 to week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	40		
Units: Number				
Any AEs	54	28		
Grade 1	36	18		
Grade 2	20	12		
Grade 3-4	5	5		
Drug related AEs	1	5		
Drug related grade 3-4 AEs	0	0		
AEs leading to the study drugs interruption	1	2		
Missing Grade	7	0		
Serious Adverse Events (SAEs)	5	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Virological Response at Week 96

End point title	Virological Response at Week 96

End point description:

End point type	Secondary

End point timeframe:

Week 96

End point values	Arm A - Immediate switch	Arm B - Deferred switch		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	45		
Units: Percentage				
number (confidence interval 95%)				
HIV RNA <50 copies/mL	84.2 (75.3 to 90.9)	73.3 (58.1 to 85.4)		
HIV RNA =>50 copies/mL	5.3 (1.7 to 11.9)	6.7 (1.4 to 18.3)		
No virologic data at week 96	10.5 (5.2 to 18.5)	20 (9.6 to 34.6)		

Attachments (see zip file)	FDA Snapshot Week 96.png

Statistical analyses

Statistical analysis title	ITT FDA Snapshot

Statistical analysis description:

Proportion of participants with HIV-RNA <50 copies/mL at week 96,
with the ITT FDA Snapshot method

Comparison groups	Arm B - Deferred switch v Arm A - Immediate switch
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	< 0.1
Method	Regression, Logistic
Parameter estimate	ITT FDA Snapshot
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Notes:

[3] - The two-sided 95% confidence interval of the difference in therapeutic success rate will be calculated.
The effect of study treatment will also be assessed in the mITT population using logistic regression model with treatment group adjusted for the presence of M184V mutation at baseline and CD4 count at baseline (above versus below 350 cells/µL) as well as all baseline variables potentially associated with the outcome, with univariable P-value <0.10.

Secondary: Number of drug-drug interactions

End point title	Number of drug-drug interactions[4]

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 96

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Both arms reported separately due to different timepoints reported.

End point values	Arm B - Deferred switch			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Number				
Baseline	45			
Week 48	39			
Week 96	38			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse event reporting period will be from consent until the subject's final study visit (I.e. follow-up visit or end of trial visit).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	Arm A - Immediate switch

Reporting group description:

Participants randomised to this arm switch to Dolutegravir/Rilpivirine Fixed Dose Combination (Juluca) at baseline.

Reporting group title	Arm B - Deferred switch

Reporting group description:

Subjects randomised to this arm continued on their current antiretroviral treatment until week 48 and then switched to the study IMP. They remained on the study IMP until week 96.

Serious adverse events	Arm A - Immediate switch	Arm B - Deferred switch	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 95 (10.53%)	4 / 45 (8.89%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Meningioma			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penile neoplasm			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			

alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Patella fracture			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Prostatectomy			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
pachymeningitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicidal ideation			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Pneumonia bacterial			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
covid19 pneumonia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Legionella infection			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pilonidal cyst			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical mycobacterial infection			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (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	Arm A - Immediate switch	Arm B - Deferred switch	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	84 / 95 (88.42%)	38 / 45 (84.44%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			

subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Haemangioma of skin			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Uterine leiomyoma			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Skin papilloma			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertension			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	6 / 95 (6.32%)	1 / 45 (2.22%)	
occurrences (all)	6	1	
Diastolic hypertension			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Systolic Hypertension			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Surgical and medical procedures			
Foot operation			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Skin neoplasm excision			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Acrochordon excision			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Sympathectomy			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	

Nasal operation			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Chest pain			
subjects affected / exposed	4 / 95 (4.21%)	0 / 45 (0.00%)	
occurrences (all)	4	0	
Discomfort			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Face oedema			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	5 / 95 (5.26%)	0 / 45 (0.00%)	
occurrences (all)	5	0	
Influenza like illness			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	0 / 95 (0.00%)	2 / 45 (4.44%)	
occurrences (all)	0	2	
Energy increased			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Ulcer			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Chills			

subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Mass			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Vaccination site pain			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Ill-defined disorder			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Inflammation			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Asthenia			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	3 / 95 (3.16%)	0 / 45 (0.00%)	
occurrences (all)	3	0	
Fatigue			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	3 / 95 (3.16%)	1 / 45 (2.22%)	
occurrences (all)	3	1	
Immune system disorders			
Hypersensitivity			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Seasonal allergy			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Social circumstances			
Disease risk factor			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast			

disorders			
Benign Prostatic Hyperplasia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Menstrual disorder			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Breast pain			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Prostatitis			
subjects affected / exposed	2 / 95 (2.11%)	1 / 45 (2.22%)	
occurrences (all)	2	1	
Genital lesion			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Asthma			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	2	2	
Bronchial disorder			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Cough			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	3 / 95 (3.16%)	1 / 45 (2.22%)	
occurrences (all)	3	1	
Dyspnoea			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Dyspnoea exertional			

subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 95 (1.05%)	2 / 45 (4.44%)	
occurrences (all)	1	2	
COVID-19			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Aggression			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Anxiety			
subjects affected / exposed	3 / 95 (3.16%)	2 / 45 (4.44%)	
occurrences (all)	3	2	
Depression			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	2 / 95 (2.11%)	1 / 45 (2.22%)	
occurrences (all)	2	1	
Stress			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	8 / 95 (8.42%)	1 / 45 (2.22%)	
occurrences (all)	8	1	
Loss of libido			
alternative dictionary used: MedDRA 24			

subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Mental disorder			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	3 / 95 (3.16%)	1 / 45 (2.22%)	
occurrences (all)	3	1	
Abnormal dreams			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	4 / 95 (4.21%)	1 / 45 (2.22%)	
occurrences (all)	4	1	
Depressed mood			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Investigations			
Glomerular filtration rate abnormal			
subjects affected / exposed	0 / 95 (0.00%)	2 / 45 (4.44%)	
occurrences (all)	0	2	
Blood pressure systolic increased			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Creatinine renal clearance decreased			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Blood pressure diastolic increased			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Glucose urine present			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	

Blood cholesterol increased				
alternative dictionary used: MedDRA 24				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Red blood cell analysis abnormal				
alternative dictionary used: MedDRA 24				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Blood immunoglobulin M decreased				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Viral load increased				
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)		
occurrences (all)	0	1		
Blood bilirubin				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Pathology test				
alternative dictionary used: MedDRA 24				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Mean cell haemoglobin decreased				
alternative dictionary used: MedDRA 24				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Blood phosphorus decreased				
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)		
occurrences (all)	1	1		
Vitamin D decreased				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Alanine aminotransferase increased				
alternative dictionary used: MedDRA 24				
subjects affected / exposed	8 / 95 (8.42%)	0 / 45 (0.00%)		
occurrences (all)	8	0		

Blood pressure increased			
subjects affected / exposed	3 / 95 (3.16%)	0 / 45 (0.00%)	
occurrences (all)	3	0	
Blood bilirubin increased			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Blood creatinine decreased			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Biopsy kidney			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Body temperature			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Transaminases increased			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Urine analysis abnormal			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Weight increased			
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Weight decreased			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Blood creatine phosphokinase increased			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	4 / 95 (4.21%)	2 / 45 (4.44%)	
occurrences (all)	4	5	

Blood creatinine increased			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	5 / 95 (5.26%)	0 / 45 (0.00%)	
occurrences (all)	5	0	
Glomerular filtration rate decreased			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	4 / 95 (4.21%)	2 / 45 (4.44%)	
occurrences (all)	4	2	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Exposure to communicable disease			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Dislocation of vertebra			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Limb injury			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Neck injury			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Ligament sprain			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Phlebitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Contusion			
alternative dictionary used: MedDRA 24			

subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Soft tissue injury			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Epicondylitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Joint injury			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Left ventricular hypertrophy			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	0 / 95 (0.00%)	2 / 45 (4.44%)	
occurrences (all)	0	2	
Nervous system disorders			
Radiculitis brachial			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Epilepsy			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Memory impairment			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
headache			

alternative dictionary used: MedDRA 24			
subjects affected / exposed	16 / 95 (16.84%)	2 / 45 (4.44%)	
occurrences (all)	21	2	
lethargy			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Anosmia			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Ageusia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Migraine			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	3	0	
Sciatica			
subjects affected / exposed	2 / 95 (2.11%)	2 / 45 (4.44%)	
occurrences (all)	2	2	
Restless legs syndrome			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)	
occurrences (all)	3	0	
Lymphadenopathy			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Lymphopenia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Polycythaemia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			

Tinnitus			
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Vertigo			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Ocular hyperaemia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Visual impairment			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
abdominal pain			
subjects affected / exposed	3 / 95 (3.16%)	1 / 45 (2.22%)	
occurrences (all)	3	1	
Anal fissure			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
anal fistula			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			
subjects affected / exposed	2 / 95 (2.11%)	1 / 45 (2.22%)	
occurrences (all)	2	1	
constipation			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	6 / 95 (6.32%)	0 / 45 (0.00%)	
occurrences (all)	7	0	
Diarrhoea			

subjects affected / exposed	6 / 95 (6.32%)	4 / 45 (8.89%)		
occurrences (all)	6	4		
Jejunal ulcer				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Dry mouth				
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)		
occurrences (all)	2	0		
Steatorrhoea				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
flatulence				
subjects affected / exposed	3 / 95 (3.16%)	0 / 45 (0.00%)		
occurrences (all)	3	0		
gastrointestinal infection				
alternative dictionary used: MedDRA 24				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Haemorrhoids				
alternative dictionary used: MedDRA 24				
subjects affected / exposed	4 / 95 (4.21%)	0 / 45 (0.00%)		
occurrences (all)	4	0		
Dyspepsia				
subjects affected / exposed	3 / 95 (3.16%)	2 / 45 (4.44%)		
occurrences (all)	3	2		
Eructation				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Lip pain				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Odynophagia				
alternative dictionary used: MedDRA 24				
subjects affected / exposed	1 / 95 (1.05%)	2 / 45 (4.44%)		
occurrences (all)	1	2		

oesophagitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Proctalgia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Proctitis			
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Abdominal pain upper			
subjects affected / exposed	2 / 95 (2.11%)	1 / 45 (2.22%)	
occurrences (all)	2	1	
Toothache			
subjects affected / exposed	2 / 95 (2.11%)	1 / 45 (2.22%)	
occurrences (all)	2	1	
Abdominal discomfort			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Gastrointestinal disorder			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Nausea			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Proctitis gonococcal			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			

Alopecia areata			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Blister			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Skin reaction			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Eczema			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	4	0	
Onychomycosis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Pruritus			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	2 / 95 (2.11%)	1 / 45 (2.22%)	
occurrences (all)	2	1	
Hyperkeratosis			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Intertrigo			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Dermatitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Skin lesion			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Rash			

subjects affected / exposed	5 / 95 (5.26%)	0 / 45 (0.00%)	
occurrences (all)	12	0	
Seborrheic Dermatitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Alopecia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Cellulitis			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
ALBUMINURIA			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
dysuria			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Focal segmental glomerulosclerosis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Nocturia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Chromaturia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Pollakiuria			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
renal colic			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Urge incontinence			

subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Urinary incontinence			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Proteinuria			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Calculus bladder			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Periarthritis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Bursitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Neck pain			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	2 / 45 (4.44%)	
occurrences (all)	1	2	
Limb discomfort			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Arthralgia			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	5 / 95 (5.26%)	2 / 45 (4.44%)	
occurrences (all)	5	2	
Pain in extremity			

subjects affected / exposed	3 / 95 (3.16%)	3 / 45 (6.67%)	
occurrences (all)	3	3	
Back pain			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	4 / 95 (4.21%)	0 / 45 (0.00%)	
occurrences (all)	4	0	
Myalgia			
subjects affected / exposed	5 / 95 (5.26%)	1 / 45 (2.22%)	
occurrences (all)	5	1	
Muscle atrophy			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	2 / 95 (2.11%)	1 / 45 (2.22%)	
occurrences (all)	2	2	
Osteoarthritis			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Osteoporosis			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Plantar fasciitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Muscle strain			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Tendonitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Osteopenia			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	

Musculoskeletal chest pain			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Joint swelling			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Tenosynovitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Infections and infestations			
Abscess			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Muscle abscess			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Amoebiasis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Genital herpes			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	2 / 45 (4.44%)	
occurrences (all)	1	2	
Lower respiratory tract infection			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Chlamydial infection			

subjects affected / exposed	4 / 95 (4.21%)	2 / 45 (4.44%)	
occurrences (all)	6	2	
Influenza			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Nasopharyngitis			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	6 / 95 (6.32%)	5 / 45 (11.11%)	
occurrences (all)	8	7	
Rhinitis			
subjects affected / exposed	5 / 95 (5.26%)	1 / 45 (2.22%)	
occurrences (all)	5	1	
folliculitis			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Fungal skin infection			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)	
occurrences (all)	3	0	
Gastroenteritis			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	2 / 95 (2.11%)	1 / 45 (2.22%)	
occurrences (all)	2	1	
Gingivitis			
subjects affected / exposed	2 / 95 (2.11%)	0 / 45 (0.00%)	
occurrences (all)	2	0	
Gonorrhoea			
subjects affected / exposed	4 / 95 (4.21%)	1 / 45 (2.22%)	
occurrences (all)	4	2	
Oropharyngeal gonococcal infection			
alternative dictionary used: MedDRA 24			

subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Gingival abscess				
alternative dictionary used: MedDRA 24				
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)		
occurrences (all)	0	1		
Helicobacter infection				
subjects affected / exposed	2 / 95 (2.11%)	1 / 45 (2.22%)		
occurrences (all)	2	1		
Herpes virus infection				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	3	0		
Herpes simplex				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Infected bite				
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)		
occurrences (all)	0	1		
lymphogranuloma venereum				
subjects affected / exposed	3 / 95 (3.16%)	1 / 45 (2.22%)		
occurrences (all)	3	1		
Malaria				
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)		
occurrences (all)	0	1		
Oral infection				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Staphylococcal infection				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Nasal abscess				
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)		
occurrences (all)	0	1		
Oral candidiasis				

subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)		
occurrences (all)	0	1		
Ear infection				
alternative dictionary used: MedDRA 24				
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)		
occurrences (all)	0	1		
Pharyngeal chlamydia infection				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Tinea versicolour				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
pneumonia				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
COVID-19				
subjects affected / exposed	9 / 95 (9.47%)	3 / 45 (6.67%)		
occurrences (all)	9	3		
Pyelonephritis				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Respiratory tract infection				
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)		
occurrences (all)	1	0		
Sinusitis				
alternative dictionary used: MedDRA 24				
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)		
occurrences (all)	1	1		
Syphilis				
alternative dictionary used: MedDRA 24				
subjects affected / exposed	6 / 95 (6.32%)	2 / 45 (4.44%)		
occurrences (all)	8	2		
Tooth abscess				
alternative dictionary used: MedDRA 24				

subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	4 / 95 (4.21%)	1 / 45 (2.22%)	
occurrences (all)	4	1	
Urinary tract infection			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	6 / 95 (6.32%)	2 / 45 (4.44%)	
occurrences (all)	7	3	
Vaginal infection			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Viral infection			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Suspected COVID-19			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Onychomycosis			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	3 / 95 (3.16%)	0 / 45 (0.00%)	
occurrences (all)	3	0	
Cellulitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Gout			
alternative dictionary used: MedDRA 24			

subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	2	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Hypocalcaemia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Increased appetite			
subjects affected / exposed	1 / 95 (1.05%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Vitamin D deficiency			
subjects affected / exposed	6 / 95 (6.32%)	0 / 45 (0.00%)	
occurrences (all)	6	0	
Diabetes mellitus			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	0 / 95 (0.00%)	2 / 45 (4.44%)	
occurrences (all)	0	2	
Hypophosphataemia			
alternative dictionary used: MedDRA 24			
subjects affected / exposed	1 / 95 (1.05%)	1 / 45 (2.22%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 January 2021	Global amendment to update protocol V3.0 to V5.0

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/38417976