Clinical trial results:
A Phase III Multicenter, Open-Label, Randomized Study to Evaluate a Switch to MK-1439A in HIV-1-Infected Subjects Virologically Suppressed on a Regimen of a Ritonavir-boosted Protease Inhibitor and Two Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

Summary

EudraCT number	2014-005550-18
Trial protocol	DE AT DK BE IT ES FR PL
Global end of trial date	05 September 2023

Results information

Result version number	v1 (current)
This version publication date	12 September 2024
First version publication date	12 September 2024

Trial information

Trial identification

Sponsor protocol code	1439a-024

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02397096
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.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	05 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 February 2018
Global end of trial reached?	Yes
Global end of trial date	05 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The multicenter, open label, randomized study will evaluate the safety and efficacy of a switch to MK-1439A (MK-1439 [doravirine] plus lamivudine and tenofovir disoproxil fumarate) in HIV-1-infected participants virologically suppressed on a protocol-specified antiretroviral regimen. The primary hypothesis is that a switch to doravirine, tenofovir, lamivudine will be non-inferior to continuation of the regimen at Screening for 24 weeks, as assessed by the proportion of participants maintaining HIV-1 ribonucleic acid (RNA) <50 copies/mL. The Base Study results will be based on the first 48 weeks of this ongoing study.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 June 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 21
Country: Number of subjects enrolled	Australia: 17
Country: Number of subjects enrolled	Austria: 23
Country: Number of subjects enrolled	Belgium: 19
Country: Number of subjects enrolled	Canada: 19
Country: Number of subjects enrolled	Colombia: 6
Country: Number of subjects enrolled	Denmark: 22
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	Germany: 58
Country: Number of subjects enrolled	Guatemala: 10
Country: Number of subjects enrolled	Israel: 16
Country: Number of subjects enrolled	Italy: 64
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 9
Country: Number of subjects enrolled	Mexico: 30
Country: Number of subjects enrolled	New Zealand: 6
Country: Number of subjects enrolled	Peru: 7
Country: Number of subjects enrolled	Poland: 29

Country: Number of subjects enrolled	Russian Federation: 43
Country: Number of subjects enrolled	Spain: 33
Country: Number of subjects enrolled	Switzerland: 22
Country: Number of subjects enrolled	United Kingdom: 51
Country: Number of subjects enrolled	United States: 142
Worldwide total number of subjects	673
EEA total number of subjects	274

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)	655
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The base study and study extension 1 were conducted at 122 centers in 23 countries. Study extension 2 was conducted at 110 centers in 23 countries. Study extension 3 was at 28 centers in 10 countries.

Pre-assignment

Screening details:

Out of 852 participants screened, 673 were randomized to study treatment, and 670 were treated.

Period 1

Period 1 title	Day 1 to Week 24
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Immediate Switch Group (ISG)

Arm description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA will switch on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Arm type	Experimental
Investigational medicinal product name	Doravirine/Lamivudine/Tenofovir
Investigational medicinal product code	
Other name	Doravirine (PIFELTRO™) Doravirine/Lamivudine/Tenofovir disoproxil fumarate (DELSTRIGO™) MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single tablet containing MK-1439 (doravirine) 100 mg, lamivudine 300 mg, and tenofovir disoproxil fumarate 300 mg

Investigational medicinal product name	Baseline regimen of antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor
Investigational medicinal product code	
Other name	Baseline regimen of atazanavir, darunavir, or lopinavir administered according to the product circular
Pharmaceutical forms	Tablet, Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

tablet, capsule or oral suspension

Investigational medicinal product name	Baseline regimen of antiretroviral therapy with two NRTIs administered according to the product circular
Investigational medicinal product code	
Other name	Baseline regimen of antiretroviral therapy with two NRTIs administered according to the product circular
Pharmaceutical forms	Tablet, Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

tablet, capsule or oral suspension

Investigational medicinal product name	Baseline regimen of antiretroviral therapy with a NNRTI (efavirenz, nevirapine, or rilpivirine) administered according to the product circular
Investigational medicinal product code	
Other name	Baseline regimen of antiretroviral therapy with a NNRTI (efavirenz, nevirapine, or rilpivirine) administered according to the product circular
Pharmaceutical forms	Tablet, Capsule, Oral solution
Routes of administration	Oral use

Dosage and administration details:

tablet, capsule or oral solution

Investigational medicinal product name	Baseline regimen of antiretroviral therapy with cobicistat-boosted elvitegravir administered according to the product circular
Investigational medicinal product code	
Other name	Baseline regimen of antiretroviral therapy with cobicistat-boosted elvitegravir administered according to the product circular
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

tablet

Arm title	Delayed Switch Group (DSG)

Arm description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they will switch to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Arm type	Active comparator
Investigational medicinal product name	Baseline regimen of antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor
Investigational medicinal product code	
Other name	Baseline regimen of atazanavir, darunavir, or lopinavir administered according to the product circular
Pharmaceutical forms	Tablet, Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

tablet, capsule or oral suspension

Investigational medicinal product name	Baseline regimen of antiretroviral therapy with two NRTIs administered according to the product circular
Investigational medicinal product code	
Other name	Baseline regimen of antiretroviral therapy with two NRTIs administered according to the product circular
Pharmaceutical forms	Tablet, Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

tablet, capsule or oral suspension

Investigational medicinal product name	Baseline regimen of antiretroviral therapy with a NNRTI (efavirenz, nevirapine, or rilpivirine) administered according to the product circular
Investigational medicinal product code	
Other name	Baseline regimen of antiretroviral therapy with a NNRTI (efavirenz, nevirapine, or rilpivirine) administered according to the product circular
Pharmaceutical forms	Tablet, Capsule, Oral suspension
Routes of administration	Oral use

Dosage and administration details: tablet, capsule, or oral suspension	
Investigational medicinal product name	Baseline regimen of antiretroviral therapy with cobicistat-boosted elvitegravir administered according to the product circular
Investigational medicinal product code	
Other name	Baseline regimen of antiretroviral therapy with cobicistat-boosted elvitegravir administered according to the product circular
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
tablet

Number of subjects in period 1	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)
Started	450	223
Treated	447	223
Completed	427	209
Not completed	23	14
Adverse event, serious fatal	1	-
Physician decision	2	3
Consent withdrawn by subject	6	1
Adverse event, non-fatal	7	1
Lost to follow-up	3	4
Randomized, not treated	3	-
Protocol deviation	1	4
Lack of efficacy	-	1

Period 2

Period 2 title	Week 24 to Week 48
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Immediate Switch Group (ISG)

Arm description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA will switch on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Arm type	Experimental
Investigational medicinal product name	Doravirine/Lamivudine/Tenofovir
Investigational medicinal product code	
Other name	Doravirine (PIFELTRO™) Doravirine/Lamivudine/Tenofovir disoproxil fumarate (DELSTRIGO™) MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single tablet containing MK-1439 (doravirine) 100 mg, lamivudine 300 mg, and tenofovir disoproxil fumarate 300 mg

Arm title	Delayed Switch Group (DSG)

Arm description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they will switch to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Arm type	Active comparator
Investigational medicinal product name	Doravirine/Lamivudine/Tenofovir
Investigational medicinal product code	
Other name	Doravirine (PIFELTRO™) Doravirine/Lamivudine/Tenofovir disoproxil fumarate (DELSTRIGO™) MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single tablet containing MK-1439 (doravirine) 100 mg, lamivudine 300 mg, and tenofovir disoproxil fumarate 300 mg

Number of subjects in period 2	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)
Started	427	209
Completed	407	202
Not completed	20	7
Physician decision	2	1
Consent withdrawn by subject	5	2
Adverse event, non-fatal	6	2
Non-Compliance With Study Drug	-	1
Lost to follow-up	2	-
Lack of efficacy	5	1

Period 3

Period 3 title	Study Extension 1
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Immediate Switch Group (ISG)

Arm description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA will switch on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Arm type	Experimental
Investigational medicinal product name	Doravirine/Lamivudine/Tenofovir
Investigational medicinal product code	
Other name	Doravirine (PIFELTRO™) Doravirine/Lamivudine/Tenofovir disoproxil fumarate (DELSTRIGO™) MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Doravirine (PIFELTRO™) Doravirine/Lamivudine/Tenofovir disoproxil fumarate (DELSTRIGO™) MK-1439A
Single tablet containing MK-1439 (doravirine) 100 mg, lamivudine 300 mg, and tenofovir disoproxil fumarate 300 mg

Arm title	Delayed Switch Group (DSG)

Arm description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they will switch to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Arm type	Active comparator
Investigational medicinal product name	Doravirine/Lamivudine/Tenofovir
Investigational medicinal product code	
Other name	Doravirine (PIFELTRO™) Doravirine/Lamivudine/Tenofovir disoproxil fumarate (DELSTRIGO™) MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Doravirine (PIFELTRO™) Doravirine/Lamivudine/Tenofovir disoproxil fumarate (DELSTRIGO™) MK-1439A
Single tablet containing MK-1439 (doravirine) 100 mg, lamivudine 300 mg, and tenofovir disoproxil fumarate 300 mg

Number of subjects in period 3[1]	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)
Started	398	202
Completed	357	179
Not completed	41	23
Adverse event, serious fatal	1	-
Physician decision	4	2
Consent withdrawn by subject	21	7
Adverse event, non-fatal	7	5
Non-Compliance With Study Drug	3	-
Pregnancy	1	-
Lost to follow-up	2	3
Lack of efficacy	2	5
Protocol deviation	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Number started refers only to participants completing Base Study and volunteering to continue to Study Extension Part 1.

Period 4

Period 4 title	Study Extension 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Immediate Switch Group (ISG)

Arm description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA will switch on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Arm type	Experimental
Investigational medicinal product name	Doravirine/Lamivudine/Tenofovir
Investigational medicinal product code	
Other name	Doravirine (PIFELTRO™) Doravirine/Lamivudine/Tenofovir disoproxil fumarate (DELSTRIGO™) MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single tablet containing MK-1439 (doravirine) 100 mg, lamivudine 300 mg, and tenofovir disoproxil fumarate 300 mg

Arm title	Delayed Switch Group (DSG)

Arm description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease

inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they will switch to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Arm type	Active comparator
Investigational medicinal product name	Doravirine/Lamivudine/Tenofovir
Investigational medicinal product code	
Other name	Doravirine (PIFELTRO™) Doravirine/Lamivudine/Tenofovir disoproxil fumarate (DELSTRIGO™) MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single tablet containing MK-1439 (doravirine) 100 mg, lamivudine 300 mg, and tenofovir disoproxil fumarate 300 mg

Number of subjects in period 4[2]	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)
Started	303	154
Completed	129	78
Not completed	174	76
Availability of study medication locally	152	64
Adverse event, serious fatal	2	-
Physician decision	2	5
Consent withdrawn by subject	10	3
Adverse event, non-fatal	3	3
Non-Compliance With Study Drug	1	-
Pregnancy	1	-
Lost to follow-up	2	1
Lack of efficacy	1	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Number started refers only to participants completing Base Study, Study Extension Part 1, and volunteering to continue to Study Extension Part 2.

Period 5

Period 5 title	Study Extension 3
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Immediate Switch Group (ISG)

Arm description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA will switch on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Arm type	Experimental
Investigational medicinal product name	Doravirine/Lamivudine/Tenofovir
Investigational medicinal product code	
Other name	Doravirine (PIFELTRO™) Doravirine/Lamivudine/Tenofovir disoproxil fumarate (DELSTRIGO™) MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single tablet containing MK-1439 (doravirine) 100 mg, lamivudine 300 mg, and tenofovir disoproxil fumarate 300 mg

Arm title	Delayed Switch Group (DSG)

Arm description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they will switch to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Arm type	Active comparator
Investigational medicinal product name	Doravirine/Lamivudine/Tenofovir
Investigational medicinal product code	
Other name	Doravirine (PIFELTRO™) Doravirine/Lamivudine/Tenofovir disoproxil fumarate (DELSTRIGO™) MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single tablet containing MK-1439 (doravirine) 100 mg, lamivudine 300 mg, and tenofovir disoproxil fumarate 300 mg

Number of subjects in period 5[3]	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)
Started	84	43
Completed	69	39
Not completed	15	4
Availability of study medication locally	11	3
Consent withdrawn by subject	2	1
Adverse event, non-fatal	1	-
Lost to follow-up	1	-

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Number started refers only to participants completing Base Study, Study Extension Part 1, Study Extension Part 2 and volunteering to continue to Study Extension Part 3.

Baseline characteristics

Reporting groups	
Reporting group title	Immediate Switch Group (ISG)
Reporting group description:	
Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA will switch on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.	
Reporting group title	Delayed Switch Group (DSG)
Reporting group description:	
Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they will switch to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.	

Reporting group values	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)	Total
Number of subjects	450	223	673
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)	441	214	655
From 65-84 years	9	9	18
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	43.1	43.7	
standard deviation	± 10.1	± 10.6	-
Sex: Female, Male Units:			
Female	75	29	104
Male	375	194	569
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	5	2	7
Asian	17	8	25
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	56	34	90
White	346	168	514
More than one race	25	11	36

Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	98	43	141
Not Hispanic or Latino	347	177	524
Unknown or Not Reported	5	3	8

End points

End points reporting groups

Reporting group title	Immediate Switch Group (ISG)

Reporting group description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA will switch on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	Delayed Switch Group (DSG)

Reporting group description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they will switch to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	Immediate Switch Group (ISG)

Reporting group description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA will switch on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	Delayed Switch Group (DSG)

Reporting group description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they will switch to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	Immediate Switch Group (ISG)

Reporting group description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA will switch on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	Delayed Switch Group (DSG)

Reporting group description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they will switch to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	Immediate Switch Group (ISG)

Reporting group description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA will switch on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	Delayed Switch Group (DSG)

Reporting group description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they will switch to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	Immediate Switch Group (ISG)

Reporting group description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA will switch on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	Delayed Switch Group (DSG)

Reporting group description:

Participants receiving continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they will switch to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Subject analysis set title	Immediate Switch (Ritonavir--boosted, PI-based) Group (ISG)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants receiving continuous antiretroviral therapy with a ritonavir-boosted, PI-based regimen for >=6 months with undetectable HIV-1 RNA will switch on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Subject analysis set title	Delayed Switch (Ritonavir-boosted, PI-based) Group (DSG)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants receiving continuous antiretroviral therapy with a ritonavir-boosted, PI-based regimen for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they will switch to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Subject analysis set title	Immediate Switch (Ritonavir--boosted, PI-based) Group (ISG)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants receiving continuous antiretroviral therapy with a ritonavir-boosted, PI-based regimen for >=6 months with undetectable HIV-1 RNA will switch on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Subject analysis set title	Delayed Switch (Ritonavir-boosted, PI-based) Group (DSG)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants receiving continuous antiretroviral therapy with a ritonavir-boosted, PI-based regimen for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they will switch to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Primary: Percentage of Participants Maintaining Human Immunodeficiency Virus–1 Ribonucleic Acid (HIV-1 RNA) <40 Copies/mL

End point title	Percentage of Participants Maintaining Human Immunodeficiency Virus–1 Ribonucleic Acid (HIV-1 RNA) <40 Copies/mL

End point description:

The percentage of participants in each arm achieving HIV-1 RNA levels <40 copies/mL was determined. Plasma HIV-1 RNA levels were quantified with the Abbott RealTime HIV-1 Assay. Data were handled according to the US Food and Drug Administration (FDA) "snapshot" approach and all missing data were

considered treatment failures, regardless of the reason. The analysis population consisted of all randomized participants who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

Immediate Switch to MK-1439A arm: Week 48; Delayed Switch to MK-1439A arm: Week 24

End point values	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	447	223		
Units: Percentage of Participants				
number (not applicable)	89.7	93.3		

Statistical analyses

Statistical analysis title	ISG, DSG
Comparison groups	Immediate Switch Group (ISG) v Delayed Switch Group (DSG)
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-3.556
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.977
upper limit	0.864

Secondary: Mean Change from Baseline in Fasting Low-density Lipoprotein Cholesterol (LDL-C)

End point title	Mean Change from Baseline in Fasting Low-density Lipoprotein Cholesterol (LDL-C)

End point description:

To evaluate the effect on fasting LDL-C of an immediate switch to DOR/3TC/TDF on Study Day 1 compared with continuation of a ritonavir-boosted, PI-based regimen, as measured by mean change from baseline in each treatment group. The Last Observation Carry Forward (LOCF) approach was applied to missing data and data collected after a participant-initiated lipid-modifying therapy. The analysis population consisted of all randomized participants in the ritonavir-boosted PI-based regimen who received at least 1 dose of study drug and had a measurement at baseline and had at least one post baseline time point assessed.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Immediate Switch (Ritonavir--boosted, PI-based) Group (ISG)	Delayed Switch (Ritonavir-boosted, PI-based) Group (DSG)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	256	125		
Units: mg/dL				
arithmetic mean (standard deviation)				
Baseline	108.82 (± 34.21)	109.00 (± 33.58)		
Change from Baseline	-16.54 (± 23.10)	-1.94 (± 25.74)		

Statistical analyses

Statistical analysis title	ISG, DSG
Comparison groups	Immediate Switch (Ritonavir--boosted, PI-based) Group (ISG) v Delayed Switch (Ritonavir-boosted, PI-based) Group (DSG)
Number of subjects included in analysis	381
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	-14.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.92
upper limit	-10.38

Secondary: Mean Change from Baseline in Fasting Non-high-density Lipoprotein Cholesterol (non-HDL-C)

End point title	Mean Change from Baseline in Fasting Non-high-density Lipoprotein Cholesterol (non-HDL-C)

End point description:

Serum non-HDL-C was determined after an overnight fast. Change from Baseline was analyzed using ANCOVA models with terms for Baseline lipid level and treatment group. The Last Observation Carry Forward (LOCF) approach was applied for missing data or data collected after modifying lipid lowering therapy. The analysis population consisted of all randomized participants in the ritonavir-boosted PI-based regimen who received at least 1 dose of study drug and had a measurement at baseline and had at least one post baseline time point assessed.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Immediate Switch (Ritonavir--boosted, PI-based) Group (ISG)	Delayed Switch (Ritonavir-boosted, PI-based) Group (DSG)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	266	133		
Units: mg/dL				
arithmetic mean (standard deviation)				
Baseline	139.14 (± 42.12)	137.99 (± 38.46)		
Change from Baseline	-24.74 (± 29.26)	-1.31 (± 28.45)		

Statistical analyses

Statistical analysis title	ISG, DSG
Comparison groups	Immediate Switch (Ritonavir--boosted, PI-based) Group (ISG) v Delayed Switch (Ritonavir-boosted, PI-based) Group (DSG)
Number of subjects included in analysis	399
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Treatment Difference
Point estimate	-23.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28
upper limit	-18.05

Secondary: Percentage of Participants Maintaining HIV-1 RNA <50 Copies/mL

End point title	Percentage of Participants Maintaining HIV-1 RNA <50 Copies/mL

End point description:

The percentage of participants in each arm achieving HIV-1 RNA levels <50 copies/mL was determined. Plasma HIV-1 RNA levels were quantified with the Abbott RealTime HIV-1 Assay. Data were handled according to the US Food and Drug Administration (FDA) "snapshot" approach and all missing data were considered treatment failures, regardless of the reason. The analysis population consisted of all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 24

End point values	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	447	223		
Units: Percentage of Participants				
number (not applicable)	93.7	94.6		

Statistical analyses

Statistical analysis title	ISG, DSG
Comparison groups	Immediate Switch Group (ISG) v Delayed Switch Group (DSG)
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Treatment Difference
Point estimate	-0.877
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.706
upper limit	2.952

Notes:

[1] - DOR/3TC/TDF QD ISG is concluded to be non-inferior to baseline regimen DSG if the lower bound of the 95% CI for the difference in percent response is above -8 percentage points.

Secondary: Mean Change from Baseline in Cluster of Differentiation (CD4) Cell Counts

End point title	Mean Change from Baseline in Cluster of Differentiation (CD4) Cell Counts

End point description:

The mean change from baseline in CD4 cell counts was assessed using the Observed Failure (OF) approach. With the OF approach, baseline values were carried forward for participants who discontinued due to lack of efficacy. Cell counts were measured and expressed as cells/mm^3, and percent change was then calculated. CD4 cell counts were quantified by a central laboratory using a commercially available assay. The analysis population consisted of all randomized participants who received at least 1 dose of study drug and had a measurement at baseline and had at least one post baseline time point assessed.

End point type	Secondary

End point timeframe:

Immediate Switch to MK-1439A arm: Baseline and Week 48; Delayed Switch to MK-1439A arm: Baseline and Week 24

End point values	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402	209		
Units: cells/mm^3				
arithmetic mean (standard deviation)				
Baseline	660.5 (± 293.4)	655.6 (± 279.3)		
Change from Baseline	13.9 (± 168.1)	18.0 (± 157.7)		

Statistical analyses

Statistical analysis title	ISG, DSG
Comparison groups	Immediate Switch Group (ISG) v Delayed Switch Group (DSG)
Number of subjects included in analysis	611
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.6
upper limit	23.5

Secondary: Mean Change from Baseline in Cluster of Differentiation (CD4) Cell Counts up to Week 24

End point title	Mean Change from Baseline in Cluster of Differentiation (CD4) Cell Counts up to Week 24

End point description:

The mean change from baseline in CD4 cell counts at Week 48 was assessed using the Observed Failure (OF) approach. With the OF approach, baseline values were carried forward for participants who discontinued due to lack of efficacy. Cell counts were measured and expressed as cells/mm^3, and percent change was then calculated. CD4 cell counts were quantified by a central laboratory using a commercially available assay. The analysis population consisted of all randomized participants who received at least 1 dose of study drug and had a measurement at baseline and had at least one post baseline time point assessed.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	412	209		
Units: cells/mm^3				
geometric mean (standard deviation)				
Baseline	664.5 (± 300.7)	655.6 (± 279.3)		
Change from Baseline	5.1 (± 174.9)	18.0 (± 157.7)		

Statistical analyses

Statistical analysis title	ISG, DSG
Comparison groups	Immediate Switch Group (ISG) v Delayed Switch Group (DSG)
Number of subjects included in analysis	621
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-12.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.1
upper limit	15.4

Secondary: Percentage of Participants Maintaining HIV-1 RNA <40 Copies/mL up to Week 24

End point title	Percentage of Participants Maintaining HIV-1 RNA <40 Copies/mL up to Week 24

End point description:

To evaluate the immunological effect of an immediate switch to MK -1439A on Study Day 1 compared with continuation of a ritonavir boosted, PI-based regimen, as measured by the proportion of subjects maintaining HIV-1 RNA below the limit of quantification (BLoQ) by the Abbott RealTime HIV-1 Assay (<40 copies/mL) in both treatment groups. The analysis population consisted of all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Immediate Switch to MK-1439A arm: Week 24; Delayed Switch to MK-1439A arm: Week 24

End point values	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	447	223		
Units: Percentage of Participants				
number (not applicable)	92.8	93.3		

Statistical analyses

Statistical analysis title	ISG, DSG
Comparison groups	Immediate Switch Group (ISG) v Delayed Switch Group (DSG)
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-0.427
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.591
upper limit	3.738

Secondary: Percentage of Participants with HIV-1 RNA >=50 Copies/mL

End point title	Percentage of Participants with HIV-1 RNA >=50 Copies/mL

End point description:

The percentage of participants in each arm achieving HIV-1 RNA levels >=50 copies/mL was determined. Plasma HIV-1 RNA levels were quantified with the Abbott RealTime HIV-1 Assay. Data were handled according to the US Food and Drug Administration (FDA) "snapshot" approach. The analysis population consisted of all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Immediate Switch to MK-1439A arm: Week 48; Delayed Switch to MK-1439A arm: Week 24

End point values	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	447	223		
Units: Percentage of Participants				
number (not applicable)	1.6	1.8		

Statistical analyses

Statistical analysis title	ISG, DSG
Comparison groups	Immediate Switch Group (ISG) v Delayed Switch Group (DSG)

Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Treatment Difference
Point estimate	-0.232
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.529
upper limit	2.064

Notes:

[2] - DOR/3TC/TDF QD ISG is concluded to be non-inferior to baseline regimen DSG if the lower bound of the 95% CI for the difference in percent response is above -4 percentage points.

Secondary: Percentage of Participants Experiencing ≥1 Adverse Event (AE)

End point title	Percentage of Participants Experiencing ≥1 Adverse Event (AE)

End point description:

An AE is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. The analysis population consisted of all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Up to week 24

End point values	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	447	223		
Units: Percentage of Participants				
number (not applicable)	68.9	52.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing ≥1 Serious Adverse Event (SAE)

End point title	Percentage of Participants Experiencing ≥1 Serious Adverse Event (SAE)

End point description:

A serious adverse event is an AE that results in death, is life threatening, results in persistent or significant disability or incapacity, results in or prolongs a hospitalization, is a congenital anomaly or birth defect, is a cancer, is associated with an overdose, or is another important medical event. The percentage of participants with any SAE was assessed. The analysis population consisted of all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	447	223		
Units: Percentage of Participants				
number (not applicable)	2.9	3.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Discontinuing From Study Medication Due to an AE(s)

End point title	Percentage of Participants Discontinuing From Study Medication Due to an AE(s)

End point description:

An AE is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. The analysis population consisted of all randomized participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	Immediate Switch Group (ISG)	Delayed Switch Group (DSG)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	447	223		
Units: Percentage of Participants				
number (not applicable)	2.5	0.4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to ~338 weeks

Adverse event reporting additional description:

All cause-mortality was reported on all allocated participants. Serious and non-serious AEs were reported for all allocated participants who received ≥1 dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	ISG Base Study Weeks 0-24

Reporting group description:

Participants received continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA switched on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	ISG Base Study Weeks 24-48

Reporting group description:

Participants received continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA switched on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	DSG Base Study Weeks 24-48

Reporting group description:

Participants received continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they switched to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	DSG Base Study Weeks 0-24

Reporting group description:

Participants received continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they switched to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	ISG Study Extension 1

Reporting group description:

Participants received continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA switched on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	DSG Study Extension 2

Reporting group description:

Participants received continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-

1 RNA will continue on this therapy until Week 24, at which time they switched to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	DSG Study Extension 1

Reporting group description:

Participants received continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they switched to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	ISG Study Extension 2

Reporting group description:

Participants received continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA switched on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	ISG Study Extension 3

Reporting group description:

Participants received continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a non nucleoside reverse transcriptase inhibitor (NNRTI) (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 (nuceloside/nucleotide reverse transcriptase inhibitors) NRTIs for >=6 months with undetectable HIV-1 RNA switched on Day 1 to MK-1439A single tablet by mouth once daily for 48 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Reporting group title	DSG Study Extension 3

Reporting group description:

Participants received continuous antiretroviral therapy with a ritonavir- or cobicistat-boosted protease inhibitor (atazanavir, darunavir, or lopinavir) or cobicistat-boosted elvitegravir or a NNRTI (specifically, efavirenz, nevirapine, or rilpivirine) in combination with 2 NRTIs for >=6 months with undetectable HIV-1 RNA will continue on this therapy until Week 24, at which time they switched to MK-1439A single tablet by mouth once daily for 24 weeks in the Base Study and, optionally, for up to an additional 6 years in the Study Extensions.

Serious adverse events	ISG Base Study Weeks 0-24	ISG Base Study Weeks 24-48	DSG Base Study Weeks 24-48
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 447 (2.91%)	11 / 427 (2.58%)	4 / 209 (1.91%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			

subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bowen's disease			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burkitt's lymphoma			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epstein-Barr virus associated lymphoma			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular carcinoma			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kaposi's sarcoma			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal cancer			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Ischaemia			

subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 447 (0.22%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	1 / 209 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Behaviour disorder			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 447 (0.22%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 447 (0.22%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 447 (0.22%)	1 / 427 (0.23%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 447 (0.00%)	1 / 427 (0.23%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase			

increased			
subjects affected / exposed	1 / 447 (0.22%)	1 / 427 (0.23%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 447 (0.22%)	1 / 427 (0.23%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CD4 lymphocytes decreased			
subjects affected / exposed	0 / 447 (0.00%)	1 / 427 (0.23%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	1 / 447 (0.22%)	1 / 427 (0.23%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental overdose			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	1 / 447 (0.22%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hand fracture			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	1 / 209 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 447 (0.22%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 447 (0.22%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			

subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	1 / 447 (0.22%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			

subjects affected / exposed	1 / 447 (0.22%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 447 (0.00%)	1 / 427 (0.23%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Distal intestinal obstruction syndrome			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 447 (0.22%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoperitoneum			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal ulcer haemorrhage			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 447 (0.22%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Prerenal failure			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			

subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cyst			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 447 (0.00%)	1 / 427 (0.23%)	1 / 209 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 447 (0.00%)	1 / 427 (0.23%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 447 (0.00%)	1 / 427 (0.23%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Abscess limb			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 447 (0.00%)	1 / 427 (0.23%)	1 / 209 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	0 / 447 (0.00%)	1 / 427 (0.23%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			

subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphangitis			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle abscess			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ophthalmic herpes zoster			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 447 (0.22%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 447 (0.00%)	1 / 427 (0.23%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shigella infection			
subjects affected / exposed	0 / 447 (0.00%)	1 / 427 (0.23%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syphilis			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculous pleurisy			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DSG Base Study Weeks 0-24	ISG Study Extension 1	DSG Study Extension 2
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 223 (3.59%)	37 / 398 (9.30%)	7 / 154 (4.55%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 223 (0.00%)	3 / 398 (0.75%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bowen's disease			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burkitt's lymphoma			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epstein-Barr virus associated lymphoma			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular carcinoma			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kaposi's sarcoma			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	1 / 223 (0.45%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal cancer			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Ischaemia			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Shock haemorrhagic			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 223 (0.00%)	2 / 398 (0.50%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 223 (0.45%)	2 / 398 (0.50%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	1 / 223 (0.45%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders			
Behaviour disorder			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 223 (0.45%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	1 / 223 (0.45%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CD4 lymphocytes decreased			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental overdose			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hip fracture			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			

subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Distal intestinal obstruction syndrome			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Haemoperitoneum			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal ulcer haemorrhage			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Prerenal failure			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			

subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cyst			
subjects affected / exposed	1 / 223 (0.45%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 223 (0.45%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 223 (0.00%)	2 / 398 (0.50%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 223 (0.00%)	2 / 398 (0.50%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Appendicitis			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	1 / 154 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphangitis			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle abscess			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ophthalmic herpes zoster			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 223 (1.35%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shigella infection			

subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syphilis			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculous pleurisy			
subjects affected / exposed	1 / 223 (0.45%)	0 / 398 (0.00%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 223 (0.00%)	1 / 398 (0.25%)	0 / 154 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DSG Study Extension 1	ISG Study Extension 2	ISG Study Extension 3
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 202 (6.44%)	13 / 303 (4.29%)	3 / 84 (3.57%)
number of deaths (all causes)	0	3	0
number of deaths resulting from adverse events	0	3	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bowen's disease			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Burkitt's lymphoma			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epstein-Barr virus associated lymphoma			
subjects affected / exposed	1 / 202 (0.50%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular carcinoma			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kaposi's sarcoma			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal cancer			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vascular disorders			
Ischaemia			
subjects affected / exposed	1 / 202 (0.50%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Behaviour disorder			

subjects affected / exposed	1 / 202 (0.50%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CD4 lymphocytes decreased			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	1 / 202 (0.50%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental overdose			
subjects affected / exposed	1 / 202 (0.50%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			

subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	1 / 202 (0.50%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			

subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 202 (0.50%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Distal intestinal obstruction syndrome			
subjects affected / exposed	1 / 202 (0.50%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Haemoperitoneum			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal ulcer haemorrhage			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Prerenal failure			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			

subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cyst			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Appendicitis			
subjects affected / exposed	2 / 202 (0.99%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Chronic sinusitis			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	1 / 202 (0.50%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphangitis			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle abscess			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ophthalmic herpes zoster			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 202 (0.99%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 202 (0.00%)	1 / 303 (0.33%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shigella infection			

subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syphilis			
subjects affected / exposed	1 / 202 (0.50%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculous pleurisy			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 202 (0.00%)	0 / 303 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DSG Study Extension 3		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 43 (2.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bowen's disease			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Burkitt's lymphoma				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epstein-Barr virus associated lymphoma				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatocellular carcinoma				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Kaposi's sarcoma				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngeal cancer				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Ischaemia				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Shock haemorrhagic				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cough			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Behaviour disorder			

subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychotic disorder				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Amylase increased				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood creatine phosphokinase increased				

subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CD4 lymphocytes decreased				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lipase increased				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Ankle fracture				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Accidental overdose				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clavicle fracture				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foot fracture				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hand fracture				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				

subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	1 / 43 (2.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina pectoris				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				

subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Amyotrophic lateral sclerosis				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lacunar infarction				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				

subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Iron deficiency anaemia				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anaemia				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Retinal detachment				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Constipation				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Distal intestinal obstruction syndrome				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Haemoperitoneum				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal ulcer haemorrhage				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Rash maculo-papular				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Prerenal failure				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				

subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal cyst				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc disorder				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abscess limb				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Appendicitis				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic sinusitis				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocarditis				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis A				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				

subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphangitis				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscle abscess				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Necrotising fasciitis				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ophthalmic herpes zoster				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus infection				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 43 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Shigella infection				

subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syphilis			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tuberculous pleurisy			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	ISG Base Study Weeks 0-24	ISG Base Study Weeks 24-48	DSG Base Study Weeks 24-48
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 447 (22.37%)	63 / 427 (14.75%)	33 / 209 (15.79%)
Nervous system disorders			
Headache			
subjects affected / exposed	29 / 447 (6.49%)	11 / 427 (2.58%)	14 / 209 (6.70%)
occurrences (all)	32	11	14
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	20 / 447 (4.47%)	13 / 427 (3.04%)	9 / 209 (4.31%)
occurrences (all)	21	13	10
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	14 / 447 (3.13%)	8 / 427 (1.87%)	3 / 209 (1.44%)
occurrences (all)	14	9	5
Back pain			

subjects affected / exposed	9 / 447 (2.01%)	16 / 427 (3.75%)	1 / 209 (0.48%)
occurrences (all)	9	16	1
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 447 (0.00%)	0 / 427 (0.00%)	0 / 209 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	33 / 447 (7.38%)	19 / 427 (4.45%)	9 / 209 (4.31%)
occurrences (all)	34	21	10

Non-serious adverse events	DSG Base Study Weeks 0-24	ISG Study Extension 1	DSG Study Extension 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 223 (12.56%)	107 / 398 (26.88%)	11 / 154 (7.14%)
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 223 (2.24%)	22 / 398 (5.53%)	3 / 154 (1.95%)
occurrences (all)	5	24	5
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 223 (2.24%)	18 / 398 (4.52%)	0 / 154 (0.00%)
occurrences (all)	5	20	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 223 (2.24%)	21 / 398 (5.28%)	1 / 154 (0.65%)
occurrences (all)	5	23	1
Back pain			
subjects affected / exposed	4 / 223 (1.79%)	21 / 398 (5.28%)	2 / 154 (1.30%)
occurrences (all)	4	22	2
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 223 (0.00%)	0 / 398 (0.00%)	6 / 154 (3.90%)
occurrences (all)	0	0	6
Nasopharyngitis			
subjects affected / exposed	12 / 223 (5.38%)	51 / 398 (12.81%)	2 / 154 (1.30%)
occurrences (all)	14	68	3

Non-serious adverse events	DSG Study Extension 1	ISG Study Extension 2	ISG Study Extension 3

Total subjects affected by non-serious adverse events subjects affected / exposed	57 / 202 (28.22%)	24 / 303 (7.92%)	9 / 84 (10.71%)
Nervous system disorders Headache subjects affected / exposed occurrences (all)	13 / 202 (6.44%) 16	2 / 303 (0.66%) 3	0 / 84 (0.00%) 0
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	11 / 202 (5.45%) 14	3 / 303 (0.99%) 3	1 / 84 (1.19%) 1
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	4 / 202 (1.98%) 4 9 / 202 (4.46%) 11	5 / 303 (1.65%) 5 7 / 303 (2.31%) 7	1 / 84 (1.19%) 1 0 / 84 (0.00%) 0
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 202 (0.00%) 0 29 / 202 (14.36%) 54	4 / 303 (1.32%) 4 5 / 303 (1.65%) 5	7 / 84 (8.33%) 7 0 / 84 (0.00%) 0

Non-serious adverse events	DSG Study Extension 3		
Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 43 (6.98%)		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0		
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0 0 / 43 (0.00%) 0		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 43 (6.98%) 3 0 / 43 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 May 2015	Amendment 1 was implemented to modify exclusion criterion #4b to include the mutations D67N and K70R in the list of excluded mutations as these 2 mutations confer decreased susceptibility to NRTIs and to clarify single mutations or components of double or triple mutations in the DOR resistance mutation list.
03 June 2015	Amendment 2 was implemented to change the PK/PD evaluation from an exploratory objective to a secondary objective given its importance in supporting the assessment of the exposure-response relationship for safety and efficacy in long-term use of DOR/3TC/TDF.
12 August 2015	Amendment 3 was implemented to add text to explain the rationale for the selected doses of the lamivudine and TDF components of DOR/3TC/TDF.
10 December 2015	Amendment 4 was implemented to add a secondary objective to evaluate the antiretroviral activity of an immediate switch to DOR/3TC/TDF on Study Day 1 compared with continuation of a ritonavir-boosted PI based-regimen for 24 weeks, as measured by the proportion of participants with HIV-1 RNA ≥50 copies/mL (ie, viral rebound) at Study Week 48 in the ISG and at Study Week 24 in the DSG based on the FDA snapshot approach.
06 May 2016	Amendment 5 was implemented to add open-label study extension 1 for 2 years to collect long-term efficacy and safety data.
01 August 2016	Amendment 6 was implemented to expand subject population by allowing enrollment of participants on InSTIs (specifically, EVG) and NNRTIs (specifically, EFV, NVP, or RPV) and use of cobicistat as a booster for PIs in order to better reflect the real-world use of various antiretroviral agents and current HIV treatment guidelines.
06 March 2018	Amendment 7 was implemented to add open-label study extension 2 to provide continued access to DOR/3TC/TDF until the drug is available locally in countries participating in the trial or for an additional 2 years (whichever comes first).
20 December 2019	Amendment 8 was implemented to extend the trial to (1) provide continued access to MK-1439A for participants who are deriving benefit from MK-1439A until the drug is available locally in countries participating in the trial or for an additional 2 years (whichever comes first), and (2) collect key safety information from participants who continue on MK-1439A.
06 December 2022	Amendment 10 was implemented as a country-specific amendment for Guatemala, Mexico, Peru, Australia, New Zealand, Russia, and Spain to inform regarding the Sponsor’s name and address change and updates that were made to the Code of Conduct in the previous amendment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported