Clinical trial results:
A Phase 2a, Randomized, Active-Comparator-Controlled, Open-Label Study to Evaluate the Efficacy and Safety of Efinopegdutide (MK-6024) in Individuals With Nonalcoholic Fatty Liver Disease

Summary

EudraCT number	2020-005136-30
Trial protocol	FR ES PL IT
Global end of trial date	19 October 2022

Results information

Result version number	v1
This version publication date	26 October 2023
First version publication date	26 October 2023

Trial information

Trial identification

Sponsor protocol code	6024-001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Merck Sharp and 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	19 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 October 2022
Global end of trial reached?	Yes
Global end of trial date	19 October 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal goal of this study is to determine the efficacy of efinopegdutide in liver fat reduction in participants with NAFLD. The primary hypotheses are that efinopegdutide is superior to semaglutide, or that efinopegdutide is superior to semaglutide by at least 10% with respect to mean relative reduction from baseline in liver fat content (LFC) after 24 weeks.

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	04 August 2021
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: 17
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Israel: 24
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 6
Country: Number of subjects enrolled	Mexico: 17
Country: Number of subjects enrolled	New Zealand: 5
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Russian Federation: 6
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Taiwan: 8
Country: Number of subjects enrolled	Turkey: 5
Country: Number of subjects enrolled	Ukraine: 8
Country: Number of subjects enrolled	United States: 25
Worldwide total number of subjects	145
EEA total number of subjects	19

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)	132
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 51 clinical sites in 16 countries.

Pre-assignment

Screening details:

Participant flow as per the database cutoff date of 19OCT2022.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Efinopegdutide

Arm description:

Efinopegdutide 20 mg/mL administered by injection once weekly for 24 weeks in a dose-escalation regimen: 2.4 mg from day 1 to week 3, 5.0 mg from week 4 to 7, and 10.0 mg from week 8 to 24.

Arm type	Experimental
Investigational medicinal product name	Efinopegdutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

20 mg/mL

Arm title	Semaglutide

Arm description:

Semaglutide 1.34 mg/mL administered by injection once weekly for 24 weeks in a dose-escalation regimen: 0.25 mg from day 1 to week 3, 0.5 mg from week 4 to 7, and 1.0 mg from week 8 to 24.

Arm type	Active comparator
Investigational medicinal product name	Semaglutide 1.34 mg/mL administered by injection once weekly for
Investigational medicinal product code	
Other name	Ozempic®
Pharmaceutical forms	Solution for infusion, Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1.34 mg/mL

Number of subjects in period 1	Efinopegdutide	Semaglutide
Started	72	73
Completed	64	71
Not completed	8	2
Physician decision	1	-
Consent withdrawn by subject	6	1
Lost to follow-up	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Efinopegdutide
Reporting group description:	
Efinopegdutide 20 mg/mL administered by injection once weekly for 24 weeks in a dose-escalation regimen: 2.4 mg from day 1 to week 3, 5.0 mg from week 4 to 7, and 10.0 mg from week 8 to 24.	
Reporting group title	Semaglutide
Reporting group description:	
Semaglutide 1.34 mg/mL administered by injection once weekly for 24 weeks in a dose-escalation regimen: 0.25 mg from day 1 to week 3, 0.5 mg from week 4 to 7, and 1.0 mg from week 8 to 24.	

Reporting group values	Efinopegdutide	Semaglutide	Total
Number of subjects	72	73	145
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)	68	64	132
From 65-84 years	4	9	13
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	48.0	50.7	
standard deviation	± 11.0	± 10.9	-
Sex: Female, Male Units: Participants			
Female	39	41	80
Male	33	32	65
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	3	2	5
Asian	7	7	14
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	62	63	125
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	25	26	51
Not Hispanic or Latino	46	47	93
Unknown or Not Reported	1	0	1

Body Mass Index (BMI) Units: Kg/M^2			
arithmetic mean	35.2	33.5	
standard deviation	± 5.7	± 5.0	-
Weight Units: kg			
arithmetic mean	100.2	94.4	
standard deviation	± 18.9	± 18.9	-

End points

End points reporting groups

Reporting group title	Efinopegdutide
Reporting group description:	
Efinopegdutide 20 mg/mL administered by injection once weekly for 24 weeks in a dose-escalation regimen: 2.4 mg from day 1 to week 3, 5.0 mg from week 4 to 7, and 10.0 mg from week 8 to 24.	
Reporting group title	Semaglutide
Reporting group description:	
Semaglutide 1.34 mg/mL administered by injection once weekly for 24 weeks in a dose-escalation regimen: 0.25 mg from day 1 to week 3, 0.5 mg from week 4 to 7, and 1.0 mg from week 8 to 24.	

Primary: Mean Relative Reduction from Baseline in Liver Fat Content (LFC) Measured by Magnetic Resonance Imaging-Estimated Proton Density Fat Fraction (MRI-PDFF), Evaluated by Blinded Independent Central Review (BICR) after 24 weeks

End point title	Mean Relative Reduction from Baseline in Liver Fat Content (LFC) Measured by Magnetic Resonance Imaging-Estimated Proton Density Fat Fraction (MRI-PDFF), Evaluated by Blinded Independent Central Review (BICR) after 24 weeks
End point description:	
LFC was measured with liver images taken by MRI-PDFF and analyzed by BICR. The analysis population consisted of all randomized participants who had received at least 1 injection (including only partial) of study intervention and had at least 1 assessment. The mean relative reduction from baseline in LFC after 24 weeks of treatment is presented.	
End point type	Primary
End point timeframe:	
Baseline and up to ~24 Weeks	

End point values	Efinopegdutide	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	73		
Units: Percent Change				
least squares mean (confidence interval 90%)	72.7 (66.8 to 78.7)	42.3 (36.5 to 48.1)		

Statistical analyses

Statistical analysis title	Difference in Least Squared Means
Comparison groups	Efinopegdutide v Semaglutide

Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Difference in least squared means
Point estimate	30.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	22.1
upper limit	38.7

Primary: Number of Participants Who Experienced an Adverse Event (AE)

End point title	Number of Participants Who Experienced an Adverse Event (AE)

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. The analysis population consisted of all randomized participants who received at least 1 injection (including only partial) of study intervention. The number of participants who experienced an adverse event is presented.

End point type	Primary

End point timeframe:

Up to ~29 weeks

End point values	Efinopegdutide	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	73		
Units: Percentage of Participants				
number (not applicable)	88.9	72.6		

Statistical analyses

Statistical analysis title	Difference (Efinopegdutide – Semaglutide) in %
Comparison groups	Efinopegdutide v Semaglutide
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	difference in percentage
Point estimate	16.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.5
upper limit	29.1

Primary: Number of Participants Who Discontinued Study Intervention Due to an AE

End point title	Number of Participants Who Discontinued Study Intervention Due to an AE

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study intervention. The analysis population consisted of all randomized participants who received at least 1 injection (including only partial) of study intervention. The number of participants who discontinued study intervention due to adverse event is presented.

End point type	Primary

End point timeframe:

Up to ~24 weeks

End point values	Efinopegdutide	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	73		
Units: Percentage of Participants				
number (not applicable)	5.6	0		

Statistical analyses

Statistical analysis title	Difference (Efinopegdutide – Semaglutide) in %
Comparison groups	Efinopegdutide v Semaglutide
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	13.5

Secondary: Mean Absolute Reduction from Baseline in LFC Measured by MRI-PDFF

(evaluated by BICR) After 24 Weeks	
End point title	Mean Absolute Reduction from Baseline in LFC Measured by MRI-PDFF (evaluated by BICR) After 24 Weeks

End point description:

LFC was measured by liver images taken by MRI-PDFF and analyzed by BICR. The analysis population included all randomized participants who had received at least 1 injection (including only partial) of study intervention and had at least 1 assessment. The mean absolute reduction from baseline in LFC after 24 weeks of treatment is presented.

End point type	Secondary

End point timeframe:

Baseline and up to ~24 Weeks

End point values	Efinopegdutide	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	73		
Units: Percent Change				
least squares mean (confidence interval 90%)	14.9 (13.6 to 16.3)	8.8 (7.5 to 10.1)		

Statistical analyses

Statistical analysis title	Difference in least squared means
Comparison groups	Efinopegdutide v Semaglutide
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Difference in least squared means
Point estimate	6.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	4.6
upper limit	7.7

Secondary: Mean Percent Change from Baseline in Body Weight After 24 weeks	
End point title	Mean Percent Change from Baseline in Body Weight After 24 weeks

End point description:

Body weight in kilograms was measured using a standardized, digital scale. The analysis population included all randomized participants who had received at least 1 injection (including only partial) of study intervention and had at least 1 assessment. The mean percent change from baseline in body weight after 24 weeks is presented.

End point type	Secondary

End point timeframe:

Baseline and up to ~24 weeks

End point values	Efinopegdutide	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	73		
Units: Percent Change				
least squares mean (confidence interval 90%)	-8.5 (-9.5 to -7.5)	-7.1 (-8.1 to -6.2)		

Statistical analyses

Statistical analysis title	Difference in Least Squared Means
Comparison groups	Efinopegdutide v Semaglutide
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.085
Method	Mixed models analysis
Parameter estimate	Difference in Least Squared Means
Point estimate	-1.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.7
upper limit	-0.1

Secondary: Mean Change from Baseline in Total Cholesterol After 24 Weeks

End point title	Mean Change from Baseline in Total Cholesterol After 24 Weeks

End point description:

Fasting blood samples were collected at baseline and after 24 weeks of treatment to assess mean change in total cholesterol. The analysis population included all randomized participants who had received at least 1 injection (including only partial) of study intervention and had at least 1 assessment. The mean change in total cholesterol is presented.

End point type	Secondary

End point timeframe:

Baseline and up to ~24 weeks

End point values	Efinopegdutide	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	73		
Units: Percent Change				
least squares mean (confidence interval 90%)	-15.2 (-18.2 to -12.2)	-8.0 (-11.0 to -5.0)		

Statistical analyses

Statistical analysis title	Difference (Efinopegdutide – Semaglutide) in %
Comparison groups	Efinopegdutide v Semaglutide
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Least Squared Means
Point estimate	-7.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-11.2
upper limit	-3.1

Secondary: Mean Change from Baseline in Non-High Density Lipoprotein-Cholesterol (non-HDL-C) After 24 Weeks

End point title	Mean Change from Baseline in Non-High Density Lipoprotein-Cholesterol (non-HDL-C) After 24 Weeks

End point description:

Fasting blood samples were collected at baseline and after 24 weeks of treatment to assess mean change in non-HDL-C. The analysis population included all randomized participants who had received at least 1 injection (including only partial) of study intervention and had at least 1 assessment. The mean change in non-HDL-C is presented.

End point type	Secondary

End point timeframe:

Baseline and up to ~24 weeks

End point values	Efinopegdutide	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	73		
Units: Percent Change				
least squares mean (confidence interval 90%)	-16.8 (-20.5 to -13.0)	-11.0 (-14.8 to -7.3)		

Statistical analyses

Statistical analysis title	Difference (Efinopegdutide – Semaglutide) in %
Comparison groups	Efinopegdutide v Semaglutide
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in least squared means
Point estimate	-5.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.9
upper limit	-0.6

Secondary: Mean Change from Baseline in High Density Lipoprotein-Cholesterol (HDL-C) After 24 Weeks

End point title	Mean Change from Baseline in High Density Lipoprotein-Cholesterol (HDL-C) After 24 Weeks

End point description:

Fasting blood samples were collected at baseline and after 24 weeks of treatment to assess mean change in HDL-C. The analysis population included all randomized participants who had received at least 1 injection (including only partial) of study intervention and had at least 1 assessment. Mean change in HDL-C is presented.

End point type	Secondary

End point timeframe:

Baseline and up to ~24 weeks

End point values	Efinopegdutide	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	73		
Units: Percent Change				
least squares mean (confidence interval 90%)	-8.1 (-11.2 to -5.1)	3.6 (0.6 to 6.6)		

Statistical analyses

Statistical analysis title	Difference (Efinopegdutide – Semaglutide) in %
Comparison groups	Efinopegdutide v Semaglutide
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in least squared means
Point estimate	-11.7

Confidence interval	
level	90 %
sides	2-sided
lower limit	-15.8
upper limit	-7.7

Secondary: Mean Change from Baseline in Low Density Lipoprotein-Cholesterol (LDL-C) After 24 weeks

End point title	Mean Change from Baseline in Low Density Lipoprotein-Cholesterol (LDL-C) After 24 weeks

End point description:

Fasting blood samples were collected at baseline and after 24 weeks of treatment to assess mean change in LDL-C. The analysis population included all randomized participants who had received at least 1 injection (including only partial) of study intervention and had at least 1 assessment. The mean change in LDL-C is presented.

End point type	Secondary

End point timeframe:

Baseline and up to ~24 weeks

End point values	Efinopegdutide	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	73		
Units: Percent Change				
least squares mean (confidence interval 90%)	-13.0 (-17.4 to -8.6)	-6.9 (-11.3 to -2.6)		

Statistical analyses

Statistical analysis title	Difference (Efinopegdutide – Semaglutide) in %
Comparison groups	Efinopegdutide v Semaglutide
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in least squared means
Point estimate	-6.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-12
upper limit	-0.1

Secondary: Mean Change from Baseline in Triglycerides (TG) After 24 Weeks

End point title	Mean Change from Baseline in Triglycerides (TG) After 24

	Weeks

End point description:

Fasting blood samples were collected at baseline and after 24 weeks of treatment to assess mean change in triglycerides. The analysis population included all randomized participants who had received at least 1 injection (including only partial) of study intervention and had at least 1 assessment. The mean change in triglycerides is presented.

End point type	Secondary

End point timeframe:

Baseline and up to ~24 weeks

End point values	Efinopegdutide	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	73		
Units: Percent Change				
least squares mean (confidence interval 90%)	-30.9 (-35.6 to -25.8)	-23.3 (-28.5 to -17.7)		

Statistical analyses

Statistical analysis title	Difference (Efinopegdutide – Semaglutide) in %
Comparison groups	Efinopegdutide v Semaglutide
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in least squared means
Point estimate	-7.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-14.3
upper limit	-0.9

Secondary: Mean Change from Baseline in Apolipoprotein B (apoB) After 24 Weeks

End point title	Mean Change from Baseline in Apolipoprotein B (apoB) After 24 Weeks

End point description:

Fasting blood samples were collected at baseline and after 24 weeks of treatment to assess mean change in apoB. The analysis population included all randomized participants who had received at least 1 injection (including only partial) of study intervention and had at least 1 assessment. The mean change in apoB is presented.

End point type	Secondary

End point timeframe:

Baseline and up to ~24 weeks

End point values	Efinopegdutide	Semaglutide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	73		
Units: Percent Change				
least squares mean (confidence interval 90%)	-14.7 (-18.2 to -11.1)	-9.2 (-12.8 to -5.7)		

Statistical analyses

Statistical analysis title	Difference (Efinopegdutide – Semaglutide) in %
Comparison groups	Efinopegdutide v Semaglutide
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in least squared means
Point estimate	-5.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.4
upper limit	-0.4

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Death and adverse events up to ~29 weeks

Adverse event reporting additional description:

Every participant is counted a single time for each applicable non-serious adverse event. A system organ class appears on this report only if one or more specific non-serious adverse events in that system organ class occurred during the study period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Semaglutide

Reporting group description:

Semaglutide 1.34 mg/mL administered by injection once weekly for 24 weeks in a dose-escalation regimen: 0.25 mg from day 1 to week 3, 0.5 mg from week 4 to 7, and 1.0 mg from week 8 to 24.

Reporting group title	Efinopegdutide

Reporting group description:

Efinopegdutide 20 mg/mL administered by injection once weekly for 24 weeks in a dose-escalation regimen: 2.4 mg from day 1 to week 3, 5.0 mg from week 4 to 7, and 10.0 mg from week 8 to 24.

Serious adverse events	Semaglutide	Efinopegdutide	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 73 (1.37%)	1 / 72 (1.39%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 73 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Spinal osteoarthritis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Semaglutide	Efinopegdutide	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 73 (60.27%)	57 / 72 (79.17%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 73 (0.00%)	4 / 72 (5.56%)	
occurrences (all)	0	4	
Lipase increased			
subjects affected / exposed	3 / 73 (4.11%)	4 / 72 (5.56%)	
occurrences (all)	3	5	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 73 (2.74%)	4 / 72 (5.56%)	
occurrences (all)	2	7	
Headache			
subjects affected / exposed	5 / 73 (6.85%)	5 / 72 (6.94%)	
occurrences (all)	8	5	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 73 (8.22%)	1 / 72 (1.39%)	
occurrences (all)	6	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	3 / 73 (4.11%)	4 / 72 (5.56%)	
occurrences (all)	4	4	
Abdominal pain			
subjects affected / exposed	2 / 73 (2.74%)	9 / 72 (12.50%)	
occurrences (all)	4	15	
Abdominal pain upper			
subjects affected / exposed	1 / 73 (1.37%)	7 / 72 (9.72%)	
occurrences (all)	1	10	
Constipation			
subjects affected / exposed	4 / 73 (5.48%)	12 / 72 (16.67%)	
occurrences (all)	4	16	
Diarrhoea			
subjects affected / exposed	13 / 73 (17.81%)	12 / 72 (16.67%)	
occurrences (all)	29	32	

Dyspepsia			
subjects affected / exposed	5 / 73 (6.85%)	6 / 72 (8.33%)	
occurrences (all)	5	6	
Flatulence			
subjects affected / exposed	1 / 73 (1.37%)	4 / 72 (5.56%)	
occurrences (all)	1	4	
Gastrooesophageal reflux disease			
subjects affected / exposed	5 / 73 (6.85%)	6 / 72 (8.33%)	
occurrences (all)	6	6	
Nausea			
subjects affected / exposed	23 / 73 (31.51%)	20 / 72 (27.78%)	
occurrences (all)	36	38	
Vomiting			
subjects affected / exposed	11 / 73 (15.07%)	12 / 72 (16.67%)	
occurrences (all)	12	23	
Infections and infestations			
COVID-19			
subjects affected / exposed	10 / 73 (13.70%)	8 / 72 (11.11%)	
occurrences (all)	10	8	
Urinary tract infection			
subjects affected / exposed	2 / 73 (2.74%)	4 / 72 (5.56%)	
occurrences (all)	2	4	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	11 / 73 (15.07%)	12 / 72 (16.67%)	
occurrences (all)	13	12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2021	Amendment 2 was created primarily to add an interim analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported