Clinical trial results:
NASH EXploratory Single and COmbination Treatment (NEXSCOT): An open label, multicenter, platform study to evaluate the safety, tolerability, pharmacokinetics and efficacy of various single and combination treatments in patients with non-alcoholic fatty liver disease (NAFLD) who manifest a non-alcoholic steatohepatitis (NASH)-like biomarker phenotype.

Summary

EudraCT number	2019-000440-10
Trial protocol	DE
Global end of trial date	06 January 2022

Results information

Result version number	v2 (current)
This version publication date	14 February 2023
First version publication date	15 December 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CADPT02A12001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04147195
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.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	06 January 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 January 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the safety and tolerability of single or combination therapy during 12 weeks of treatment

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 June 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 2
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	United States: 36
Worldwide total number of subjects	41
EEA total number of subjects	3

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)	38
From 65 to 84 years	3

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from 10 sites in 3 countries.

Pre-assignment

Screening details:

Participants underwent a Screening period of up to 33 days followed by a Baseline assessment period of up to 27 days.

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	LYS006

Arm description:

LYS006 20 mg was administered orally twice per day (b.i.d) for 12 weeks

Arm type	Experimental
Investigational medicinal product name	LYS006
Investigational medicinal product code	LYS006
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LYS006 20 mg was administered orally twice per day (b.i.d) for 12 weeks

Arm title	LYS006 + LJN452

Arm description:

LYS006 20 mg was administered orally twice per day (b.i.d) in addition to LJN452 200ug administered orally once daily for 12 weeks

Arm type	Experimental
Investigational medicinal product name	LJN452
Investigational medicinal product code	LJN452
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LJN452 200ug administered orally once daily for 12 weeks

Investigational medicinal product name	LYS006
Investigational medicinal product code	LYS006
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LYS006 20 mg was administered orally twice per day (b.i.d) for 12 weeks

Number of subjects in period 1	LYS006	LYS006 + LJN452
Started	20	21
PD analysis set	20	17
Completed	16	15
Not completed	4	6
Consent withdrawn by subject	-	1
Adverse event, non-fatal	-	3
Study Terminated by Sponsor	4	2

Baseline characteristics

Reporting groups	
Reporting group title	LYS006
Reporting group description:	
LYS006 20 mg was administered orally twice per day (b.i.d) for 12 weeks	
Reporting group title	LYS006 + LJN452
Reporting group description:	
LYS006 20 mg was administered orally twice per day (b.i.d) in addition to LJN452 200ug administered orally once daily for 12 weeks	

Reporting group values	LYS006	LYS006 + LJN452	Total
Number of subjects	20	21	41
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)	19	19	38
From 65-84 years	1	2	3
85 years and over	0	0	0
Age Continuous			
Units: Year			
arithmetic mean	52.0	54.9	
standard deviation	± 9.23	± 8.36	-
Sex: Female, Male			
Units: Participants			
Female	11	11	22
Male	9	10	19
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	1	1	2
White	19	17	36
More than one race	0	1	1
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	LYS006
Reporting group description:	
LYS006 20 mg was administered orally twice per day (b.i.d) for 12 weeks	
Reporting group title	LYS006 + LJN452
Reporting group description:	
LYS006 20 mg was administered orally twice per day (b.i.d) in addition to LJN452 200ug administered orally once daily for 12 weeks	

Primary: Number of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs)[1]
End point description:	
Number of participants with AEs and SAEs including significant changes from baseline in vital signs, electrocardiograms and laboratory parameters qualifying and reported as AEs. The number of participants in each category is reported in the table.	
End point type	Primary
End point timeframe:	
From the start of treatment to 28 days after end of treatment, assessed up to maximum duration of 113 Days	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis were planned for this endpoint.

End point values	LYS006	LYS006 + LJN452		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	21		
Units: Participants				
AEs	14	17		
Treatment-related AEs	2	15		
SAEs	0	0		
AEs leading to discontinuation of study treatment	0	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Non-invasive Markers of Hepatic Fibrosis: Enhanced Liver Fibrosis Test (ELF) Score

End point title	Change From Baseline in Non-invasive Markers of Hepatic Fibrosis: Enhanced Liver Fibrosis Test (ELF) Score
End point description:	
The markers of fibrosis assessed in this test comprised hyaluronic acid (HA), tissue inhibitor of	

metalloproteinase (TIMP1) and procollagen III N-terminal peptide (PIIINP); these are components of the extracellular matrix and basement sinusoidal membrane of the liver and are elevated during fibrogenesis as a result of activation of the hepatic stellate cell. The ELF test is a composite score: < 7.7: no to mild fibrosis; ≥ 7.7 - < 9.8: Moderate fibrosis; ≥ 9.8 - < 11.3: Severe fibrosis; ≥ 11.3: Cirrhosis.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates decreased fibrosis.

End point type	Secondary

End point timeframe:

Baseline and Days 57, 85 and EOS (Day 113)

End point values	LYS006	LYS006 + LJN452		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	17		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Day 57	-0.25 (± 0.564)	0.29 (± 0.286)		
Day 85	-0.12 (± 0.780)	0.18 (± 0.687)		
EOS	0.01 (± 0.713)	0.09 (± 0.461)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Cholesterol: fasting lipid profile endpoint

End point title	Change from Baseline in Cholesterol: fasting lipid profile endpoint

End point description:

Fasting lipid profile (total cholesterol) was examined as a cardiometabolic risk parameter. Total cholesterol was measured on blood samples under fasted conditions and analyzed at a central laboratory.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates cardiovascular risk.

End point type	Secondary

End point timeframe:

Baseline and Days 15, 29, 43, 57, 85 and EOS (Day 113)

End point values	LYS006	LYS006 + LJN452		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	17		
Units: mmol / L				
arithmetic mean (standard deviation)				
Day 15	-0.025 (± 0.5814)	0.086 (± 0.8825)		
Day 29	-0.058 (± 0.6058)	0.431 (± 1.0688)		
Day 43	-0.109 (± 0.6758)	0.474 (± 1.0364)		
Day 57	-0.246 (± 0.6341)	0.463 (± 1.3026)		
Day 85	0.001 (± 0.8558)	0.754 (± 0.9915)		
EOS	-0.283 (± 1.1182)	0.249 (± 0.5175)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in percent liver fat at day 85

End point title	Change from Baseline in percent liver fat at day 85

End point description:

Percent (%) Liver fat was measured by Magnetic Resonance Imaging Proton Density Liver Fat Fraction (MRIPDFF). Participants underwent magnetic resonance imaging twice during the course of the study (baseline and end of treatment) to quantitate liver fat.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates a reduction in a component of NAFLD.

End point type	Secondary

End point timeframe:

Baseline and Day 85

End point values	LYS006	LYS006 + LJN452		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	11		
Units: Percentage of Liver Fat				
arithmetic mean (standard deviation)	-3.74 (± 3.470)	-7.52 (± 5.846)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Body Weight

End point title	Change From Baseline in Total Body Weight

End point description:

Body weight (to the nearest 0.1 kilogram [kg] was measured on a calibrated scale. The measurement was performed with the study participant in underwear and without shoes; or while wearing minimal indoor clothing.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates improvement in obesity.

End point type	Secondary

End point timeframe:

Baseline and Days 15, 29, 43, 57, 85 and EOS (Day 113)

End point values	LYS006	LYS006 + LJN452		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	17		
Units: kg				
arithmetic mean (standard deviation)				
Day 15	-0.21 (± 1.412)	-1.09 (± 2.030)		
Day 29	-0.27 (± 1.513)	-1.17 (± 2.455)		
Day 43	-0.24 (± 1.664)	-1.94 (± 2.780)		
Day 57	-0.48 (± 1.548)	-2.97 (± 3.144)		
Day 85	-0.54 (± 2.334)	-3.33 (± 2.892)		
EOS	0.17 (± 2.753)	-2.56 (± 2.789)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) at Day 85

End point title	Change from Baseline in Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) at Day 85

End point description:

HOMA-IR is a test that uses a simultaneous fasting blood glucose test and fasting insulin test to accurately estimate the degree of insulin resistance (IR) and β-cell function (the cells of the pancreas that produce insulin). HOMA-IR scores are classified as follows: Insulin sensitive is considered less than 1.0, Healthy is considered 0.5-1.4, Above 1.8 is early insulin resistance and Above 2.7 is considered significant insulin resistance

HOMA-IR= [Fasting glucose (mmol/L) x (fasting insulin (pmol/L)/6)] / 22.5

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates improvement in insulin sensitivity.

End point type	Secondary

End point timeframe:

Baseline and Day 85

End point values	LYS006	LYS006 + LJN452		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	9		
Units: HOMA-IR score				
arithmetic mean (standard deviation)	-3.74 (± 9.865)	1.67 (± 7.741)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Fasting Glucose

End point title	Change from baseline in Fasting Glucose

End point description:

Fasting Glucose was examined as a cardiometabolic risk parameter. Total fasting glucose was measured on blood samples under fasted conditions and analyzed at a central laboratory.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates improvement in glycemic control.

End point type	Secondary

End point timeframe:

Baseline and Days 15, 29, 43, 57, 85 and EOS (Day 113)

End point values	LYS006	LYS006 + LJN452		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	17		
Units: mmol / L				
arithmetic mean (standard deviation)				
Day 15	0.26 (± 2.609)	0.26 (± 2.402)		
Day 29	-0.04 (± 3.541)	0.61 (± 2.362)		
Day 43	-0.53 (± 3.655)	1.05 (± 2.449)		
Day 57	-0.82 (± 3.176)	0.84 (± 1.960)		
Day 85	-1.74 (± 3.810)	0.41 (± 2.023)		
EOS	-1.01 (± 3.627)	-0.40 (± 1.563)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fasting Insulin at Day 85

End point title	Change from Baseline in Fasting Insulin at Day 85

End point description:

Fasting insulin was examined as a cardiometabolic risk parameter. Total fasting insulin was measured on blood samples under fasted conditions and analyzed at a central laboratory.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates improvement in insulin sensitivity.

End point type	Secondary

End point timeframe:

Baseline and Day 85

End point values	LYS006	LYS006 + LJN452		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	9		
Units: pmol / L				
arithmetic mean (standard deviation)	-28.36 (± 139.23)	14.23 (± 63.875)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Hemoglobin A1c (HbA1c)

End point title	Change from baseline in Hemoglobin A1c (HbA1c)

End point description:

HbA1c was examined as a cardiometabolic risk parameter. HbA1c was measured on blood samples under fasted conditions and analyzed at a central laboratory.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates improvement in glycemic control.

End point type	Secondary

End point timeframe:

Baseline and Days 15, 29, 43, 57, 85 and EOS (Day 113)

End point values	LYS006	LYS006 + LJN452		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	17		
Units: Percentage				
arithmetic mean (standard deviation)				
Day 15	0.10 (± 0.194)	0.08 (± 0.338)		
Day 29	0.03 (± 0.431)	0.21 (± 0.487)		
Day 43	-0.02 (± 0.544)	0.31 (± 0.884)		
Day 57	-0.11 (± 0.730)	0.36 (± 0.680)		
Day 85	-0.48 (± 0.834)	-0.03 (± 0.863)		
EOS	-0.59 (± 0.961)	0.34 (± 0.359)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Alanine aminotransferase (ALT)

End point title	Change from Baseline in Alanine aminotransferase (ALT)

End point description:

Alanine aminotransferase (ALT) is an enzyme found primarily in the liver. ALT is increased with liver damage. In this study, the blood levels of ALT was used to detect liver inflammation.

Baseline is defined as the mean of the last 2 non-missing measurements taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates a reduction in liver inflammation.

End point type	Secondary

End point timeframe:

Baseline and days 15, 29, 43, 57, 85 and EOS (Day 113)

End point values	LYS006	LYS006 + LJN452		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	17		
Units: U / L				
arithmetic mean (standard deviation)				
Day 15	0.97 (± 18.255)	-19.75 (± 25.617)		
Day 29	-6.92 (± 22.166)	-9.63 (± 13.774)		
Day 43	-11.13 (± 21.624)	-8.68 (± 14.573)		

Day 57	-12.09 (± 25.401)	-17.04 (± 12.841)		
Day 85	-7.21 (± 34.702)	-11.14 (± 26.318)		
EOS	-14.50 (± 29.619)	-8.05 (± 14.570)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in High-sensitivity C-reactive Protein (hsCRP)

End point title	Change from baseline in High-sensitivity C-reactive Protein (hsCRP)

End point description:

High-sensitivity C-reactive protein is a blood test marker for inflammation in the body. HsCRP was measured from a blood sample and analyzed at a central laboratory.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates a reduction in liver inflammation.

End point type	Secondary

End point timeframe:

Baseline and Days 57, 85 and EOS (Day 113)

End point values	LYS006	LYS006 + LJN452		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	17		
Units: mg / L				
arithmetic mean (standard deviation)				
Day 57	-0.32 (± 2.192)	-7.78 (± 27.500)		
Day 85	-0.62 (± 2.180)	0.24 (± 1.692)		
EOS	0.19 (± 3.432)	0.05 (± 1.015)		

Statistical analyses

No statistical analyses for this end point

Secondary: LYS006 plasma concentration

End point title	LYS006 plasma concentration

End point description:

LYS006 plasma concentrations were determined by a validated liquid chromatography with tandem mass spectrometry (LC-MS/MS) method. No methods for imputation of missing data were used.

End point type	Secondary

End point timeframe:

pre-dose at Days 1, 29, 57 and 85 and post-dose (1, 2, 3 and 4 hours) at Days 29 and 57

End point values	LYS006	LYS006 + LJN452		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	21		
Units: ng / mL				
arithmetic mean (standard deviation)				
Day 1 (0 h)	0.162 (± 0.648)	0.00 (± 0.00)		
Day 29 (0 h)	78.9 (± 74.0)	53.5 (± 74.9)		
Day 29 (1 h)	174 (± 89.6)	169 (± 105)		
Day 29 (2 h)	224 (± 113)	189 (± 105)		
Day 29 (3 h)	188 (± 89.8)	145 (± 54.9)		
Day 29 (4 h)	149 (± 73.6)	110 (± 31.8)		
Day 57 (0 h)	58.0 (± 57.2)	24.0 (± 21.4)		
Day 57 (1 h)	200 (± 118)	123 (± 123)		
Day 57 (2 h)	222 (± 80.3)	198 (± 88.7)		
Day 57 (3 h)	188 (± 74.3)	156 (± 59.2)		
Day 57 (4 h)	140 (± 83.3)	126 (± 54.1)		
Day 85 (0 h)	15.2 (± 17.6)	10.2 (± 18.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed plasma concentration (Cmax) of LYS006

End point title	Maximum observed plasma concentration (Cmax) of LYS006

End point description:

LYS006 plasma concentrations were determined by a validated liquid chromatography with tandem mass spectrometry (LC-MS/MS) method. Cmax of LYS006 was determined with Phoenix WinNonlin (Version 8.0 or higher). No methods for imputation of missing data were used.

End point type	Secondary

End point timeframe:

pre-dose and post-dose (1, 2, 3 and 4 hours) at Days 29 and 57

End point values	LYS006	LYS006 + LJN452		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	21		
Units: ng / mL				
arithmetic mean (standard deviation)				
Day 29	264 (± 87.7)	215 (± 98.8)		
Day 57	271 (± 71.1)	228 (± 88.1)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment-emergent adverse events	
Adverse event reporting additional description:	
Any sign or symptom that occurs during the study treatment plus the 28 days post treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	LYS006
Reporting group description:	
LYS006 20 mg was administered orally twice per day (b.i.d) for 12 weeks	
Reporting group title	Total
Reporting group description:	
Total	
Reporting group title	LYS006 + LJN452
Reporting group description:	
LYS006 20 mg was administered orally twice per day (b.i.d) in addition to LJN452 200ug administered orally once daily for 12 weeks	

Serious adverse events	LYS006	Total	LYS006 + LJN452
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 41 (0.00%)	0 / 21 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	LYS006	Total	LYS006 + LJN452
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 20 (45.00%)	24 / 41 (58.54%)	15 / 21 (71.43%)
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	2 / 41 (4.88%)	2 / 21 (9.52%)
occurrences (all)	0	3	3
Alanine aminotransferase increased			

subjects affected / exposed	0 / 20 (0.00%)	2 / 41 (4.88%)	2 / 21 (9.52%)
occurrences (all)	0	2	2
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 20 (0.00%)	3 / 41 (7.32%)	3 / 21 (14.29%)
occurrences (all)	0	3	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 20 (10.00%)	2 / 41 (4.88%)	0 / 21 (0.00%)
occurrences (all)	2	2	0
Headache			
subjects affected / exposed	4 / 20 (20.00%)	8 / 41 (19.51%)	4 / 21 (19.05%)
occurrences (all)	4	8	4
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 20 (5.00%)	3 / 41 (7.32%)	2 / 21 (9.52%)
occurrences (all)	1	3	2
Diarrhoea			
subjects affected / exposed	3 / 20 (15.00%)	3 / 41 (7.32%)	0 / 21 (0.00%)
occurrences (all)	3	3	0
Nausea			
subjects affected / exposed	3 / 20 (15.00%)	5 / 41 (12.20%)	2 / 21 (9.52%)
occurrences (all)	3	5	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 20 (0.00%)	13 / 41 (31.71%)	13 / 21 (61.90%)
occurrences (all)	0	14	14
Rash			
subjects affected / exposed	0 / 20 (0.00%)	2 / 41 (4.88%)	2 / 21 (9.52%)
occurrences (all)	0	2	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 41 (4.88%)	2 / 21 (9.52%)
occurrences (all)	0	2	2
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 20 (5.00%)	4 / 41 (9.76%)	3 / 21 (14.29%)
occurrences (all)	1	4	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
10 December 2021	The study was terminated based upon an ongoing review of the study data, which showed a low likelihood of achieving required efficacy in either treatment arm.	-

Notes:

Limitations and caveats

None reported