Clinical trial results:
Evaluation of Efficacy, Safety and Tolerability of NGM282 (Aldafermin) in a Phase 2b, Randomized, Double-blind, Placebo-controlled, Multi-center Study in Subjects with Compensated Cirrhosis Due to Nonalcoholic Steatohepatitis (ALPINE 4)

Summary

EudraCT number	2019-002341-38
Trial protocol	GB DE FR BE PL
Global end of trial date	23 February 2023

Results information

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

Trial information

Trial identification

Sponsor protocol code	282-CC-207

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04210245
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	NGM Biopharmaceuticals, Inc.
Sponsor organisation address	333 Oyster Point Boulevard, San Francisco, United States, CA 94080
Public contact	NGM Study Director, NGM Biopharmaceuticals, Inc., ngm282@ngmbio.com
Scientific contact	NGM Study Director, NGM Biopharmaceuticals, Inc., ngm282@ngmbio.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	13 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 February 2023
Global end of trial reached?	Yes
Global end of trial date	23 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy and safety of aldafermin compared to placebo.

Protection of trial subjects:

This study was conducted in accordance with the protocol and with the following:
1. Ethical principles for medical subjects involving human subjects derived from the Declaration of Helsinki.
2. Applicable ICH Good Clinical Practice Guidelines.
3. Applicable laws and regulations.

Background therapy:

Not Applicable.

Evidence for comparator:

Not Applicable.

Actual start date of recruitment	23 December 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 121
Country: Number of subjects enrolled	Hong Kong: 5
Country: Number of subjects enrolled	Australia: 18
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 4
Worldwide total number of subjects	160
EEA total number of subjects	13

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	111
From 65 to 84 years	49
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 81 sites in the US (including Puerto Rico), Australia, Hong Kong, and Europe (including Belgium, France, Germany, Poland, Spain (screened the subjects, none enrolled), and the United Kingdom).

Pre-assignment

Screening details:

In total 580 subjects were screened of which 420 patients failed (367 failed randomization criteria, 22 withdrew, 3 due to adverse events, 2 lost to follow-up, 2 due to Physician decision and 24 patients for other reasons). Total 160 patients were randomized.
Note: A subject could have more than one screen-failure reason.

Period 1

Period 1 title	Overall Study (Overall period) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

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

Dosage and administration details:

Placebo matched to aldafermin will be administered as per the schedule specified in the arm.

Arm title	Aldafermin 0.3 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Aldafermin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Solution for injection

Dosage and administration details:

Doses of 0.3 mg. For Sub-Cutaneous administration daily for 48 weeks.

Arm title	Aldafermin 1 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Aldafermin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Solution for injection

Dosage and administration details:

Doses of 1 mg. For Sub-Cutaneous administration daily for 48 weeks.

Arm title	Aldafermin 3 mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Aldafermin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Solution for injection

Dosage and administration details:

Doses of 3 mg. For Sub-Cutaneous administration daily for 48 weeks.

Number of subjects in period 1	Placebo	Aldafermin 0.3 mg	Aldafermin 1 mg
Started	56	7	42
Completed	49	7	37
Not completed	7	0	5
Consent withdrawn by subject	4	-	1
Adverse event, non-fatal	-	-	3
Other	2	-	-
Lost to follow-up	1	-	1

Number of subjects in period 1	Aldafermin 3 mg
Started	55
Completed	44
Not completed	11
Consent withdrawn by subject	4
Adverse event, non-fatal	6
Other	-
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Aldafermin 0.3 mg
Reporting group description: -	
Reporting group title	Aldafermin 1 mg
Reporting group description: -	
Reporting group title	Aldafermin 3 mg
Reporting group description: -	

Reporting group values	Placebo	Aldafermin 0.3 mg	Aldafermin 1 mg
Number of subjects	56	7	42
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)	45	5	24
From 65-84 years	11	2	18
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	58.3	59.7	61.3
standard deviation	± 8.11	± 6.78	± 7.57
Gender categorical Units: Subjects			
Female	39	5	23
Male	17	2	19

Reporting group values	Aldafermin 3 mg	Total	
Number of subjects	55	160	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	37	111	
From 65-84 years	18	49	

85 years and over	0	0	

Age continuous Units: years			
arithmetic mean	59.6		
standard deviation	± 8.72	-	
Gender categorical Units: Subjects			
Female	36	103	
Male	19	57	

Subject analysis sets

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received at least 1 dose (full or partial) of study drug were included in the Safety Analysis Set. All safety endpoints are summarized using the Safety Analysis Set and were based on the actual treatment received if it differed from the randomized treatment.

Reporting group values	Safety Population		
Number of subjects	160		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	111		
From 65-84 years	49		
85 years and over	0		
Age continuous Units: years			
arithmetic mean	59.6		
standard deviation	± 8.15		
Gender categorical Units: Subjects			
Female	103		
Male	57		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Aldafermin 0.3 mg
Reporting group description: -	
Reporting group title	Aldafermin 1 mg
Reporting group description: -	
Reporting group title	Aldafermin 3 mg
Reporting group description: -	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received at least 1 dose (full or partial) of study drug were included in the Safety Analysis Set. All safety endpoints are summarized using the Safety Analysis Set and were based on the actual treatment received if it differed from the randomized treatment.

Primary: The Change from Baseline in ELF at Week 48

End point title	The Change from Baseline in ELF at Week 48[1]

End point description:

p-values were not reported for the Aldafermin 0.3 mg group versus placebo because the Aldafermin 0.3 mg treatment group was terminated during the study.

End point type	Primary

End point timeframe:

Week 48

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 0.3 mg Aldafermin was reported for safety and not for efficacy, since the 0.3 mg Aldafermin arm was discontinued and all the patients was merged with 1 mg Aldafermin.

End point values	Placebo	Aldafermin 1 mg	Aldafermin 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	37	44	
Units: ELF Score				
arithmetic mean (standard deviation)	0.263 (± 0.5767)	0.125 (± 0.6938)	-0.213 (± 0.6145)	

Statistical analyses

Statistical analysis title	Least Squares (LS) Placebo vs Aldafermin 1 mg
Comparison groups	Placebo v Aldafermin 1 mg

Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3112
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.137
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.403
upper limit	0.129
Variability estimate	Standard error of the mean
Dispersion value	0.1347

Statistical analysis title	Least Squares (LS) Placebo vs Aldafermin 3 mg
Comparison groups	Placebo v Aldafermin 3 mg
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.473
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.726
upper limit	-0.22
Variability estimate	Standard error of the mean
Dispersion value	0.128

Primary: Safety assessed by reported and observed adverse events

End point title	Safety assessed by reported and observed adverse events[2]

End point description:

End point type	Primary

End point timeframe:

48 weeks

Notes:

[2] - 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 was performed for this endpoint. The information has been introduced in the section "Adverse Events".

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	160			
Units: number of adverse events	160			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event monitoring starts from the time the patient consents to the study until they complete the trial i.e., the screening period, the double-blind treatment period of 48 weeks, and the safety follow-up period of 6-10 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Aldafermin 0.3 mg
Reporting group description: -	
Reporting group title	Aldafermin 1 mg
Reporting group description: -	
Reporting group title	Aldafermin 3 mg
Reporting group description: -	

Serious adverse events	Placebo	Aldafermin 0.3 mg	Aldafermin 1 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	11 / 42 (26.19%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	0 / 42 (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
Rectal cancer			
subjects affected / exposed	1 / 56 (1.79%)	0 / 7 (0.00%)	0 / 42 (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
Squamous cell carcinoma of head and neck			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	0 / 42 (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 of skin			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	0 / 42 (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			
Contusion			
subjects affected / exposed	1 / 56 (1.79%)	0 / 7 (0.00%)	0 / 42 (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
Femur fracture			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	0 / 42 (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 / 56 (1.79%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure acute			

subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
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 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
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			
Haematemesis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	0 / 42 (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			
Dyspnoea			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 56 (1.79%)	0 / 7 (0.00%)	0 / 42 (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			
Acute kidney injury			

subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	0 / 42 (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
Osteoarthritis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 7 (0.00%)	0 / 42 (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

Serious adverse events	Aldafermin 3 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 55 (9.09%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal cancer			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of head and neck			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femur fracture			

subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure acute			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Haematemesis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 55 (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	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			

subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Soft tissue infection			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 55 (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	Placebo	Aldafermin 0.3 mg	Aldafermin 1 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 56 (87.50%)	5 / 7 (71.43%)	40 / 42 (95.24%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0

Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	2 / 56 (3.57%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	5 / 56 (8.93%)	0 / 7 (0.00%)	6 / 42 (14.29%)
occurrences (all)	5	0	6
Injection site bruising			
subjects affected / exposed	6 / 56 (10.71%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	6	1	1
Injection site pain			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	3	0	2
Oedema peripheral			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	3	0	2
Pyrexia			
subjects affected / exposed	2 / 56 (3.57%)	0 / 7 (0.00%)	4 / 42 (9.52%)
occurrences (all)	2	0	4
Injection site erythema			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Injection site pruritus			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Immune system disorders			
Reaction to food additive			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 56 (7.14%)	1 / 7 (14.29%)	5 / 42 (11.90%)
occurrences (all)	4	1	5
Oropharyngeal pain			
subjects affected / exposed	2 / 56 (3.57%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	2	0	3
Investigations			
Blood calcium increased			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
White blood cell count increased			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 56 (1.79%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	1	0	3
Procedural pain			
subjects affected / exposed	6 / 56 (10.71%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	6	0	2
Skin laceration			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 56 (1.79%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 56 (7.14%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	4	0	2
Headache			

subjects affected / exposed	5 / 56 (8.93%)	0 / 7 (0.00%)	4 / 42 (9.52%)
occurrences (all)	5	0	4
Loss of consciousness			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Memory impairment			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	3	0	0
Neuralgia			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	3	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 56 (1.79%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Abdominal distension			
subjects affected / exposed	5 / 56 (8.93%)	1 / 7 (14.29%)	3 / 42 (7.14%)
occurrences (all)	5	1	3
Abdominal pain			
subjects affected / exposed	5 / 56 (8.93%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	5	0	2
Abdominal pain lower			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	3	0	0
Abdominal pain upper			
subjects affected / exposed	10 / 56 (17.86%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	10	0	3
Constipation			
subjects affected / exposed	7 / 56 (12.50%)	1 / 7 (14.29%)	5 / 42 (11.90%)
occurrences (all)	7	1	5
Diarrhoea			

subjects affected / exposed	10 / 56 (17.86%)	1 / 7 (14.29%)	11 / 42 (26.19%)
occurrences (all)	10	1	11
Diverticulum			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	3	0	0
Faeces discoloured			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	0	0	2
Frequent bowel movements			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	4 / 42 (9.52%)
occurrences (all)	0	0	4
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 56 (1.79%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	1	0	3
Nausea			
subjects affected / exposed	5 / 56 (8.93%)	2 / 7 (28.57%)	12 / 42 (28.57%)
occurrences (all)	5	2	12
Varices oesophageal			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	3	0	2
Hepatobiliary disorders			
Portal hypertension			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Photosensitivity reaction			

subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences (all)	3	0	1
Rash			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	3	0	2
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	3	0	0
Nephrolithiasis			
subjects affected / exposed	2 / 56 (3.57%)	1 / 7 (14.29%)	3 / 42 (7.14%)
occurrences (all)	2	1	3
Proteinuria			
subjects affected / exposed	1 / 56 (1.79%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 56 (10.71%)	0 / 7 (0.00%)	5 / 42 (11.90%)
occurrences (all)	6	0	5
Back pain			
subjects affected / exposed	4 / 56 (7.14%)	1 / 7 (14.29%)	2 / 42 (4.76%)
occurrences (all)	4	1	2
Flank pain			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences (all)	3	0	1
Muscle spasms			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences (all)	3	0	1
Muscular weakness			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			

subjects affected / exposed	4 / 56 (7.14%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	4	1	0
Neck pain			
subjects affected / exposed	1 / 56 (1.79%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Osteoarthritis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	1 / 56 (1.79%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	1	0	2
Infections and infestations			
COVID-19			
subjects affected / exposed	17 / 56 (30.36%)	1 / 7 (14.29%)	13 / 42 (30.95%)
occurrences (all)	17	1	13
Lower respiratory tract infection			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	5 / 56 (8.93%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	5	0	2
Sinusitis			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	3	0	2
Skin bacterial infection			
subjects affected / exposed	0 / 56 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 56 (1.79%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	1	1	1
Urinary tract infection			
subjects affected / exposed	9 / 56 (16.07%)	2 / 7 (28.57%)	4 / 42 (9.52%)
occurrences (all)	9	2	4
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 56 (1.79%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	1	1	0

Cellulitis			
subjects affected / exposed	1 / 56 (1.79%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	1	1	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 56 (5.36%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences (all)	3	0	1
Diabetes mellitus			
subjects affected / exposed	3 / 56 (5.36%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	3	1	1
Hypoglycaemia			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Increased appetite			
subjects affected / exposed	0 / 56 (0.00%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	0	0	2
Type 2 diabetes mellitus			
subjects affected / exposed	2 / 56 (3.57%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	2	0	3
Vitamin D deficiency			
subjects affected / exposed	2 / 56 (3.57%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	2	1	1

Non-serious adverse events	Aldafermin 3 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 55 (94.55%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	4		

General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	7 / 55 (12.73%)		
occurrences (all)	7		
Injection site bruising			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	4		
Injection site pain			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Oedema peripheral			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Injection site erythema			
subjects affected / exposed	5 / 55 (9.09%)		
occurrences (all)	5		
Injection site pruritus			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Immune system disorders			
Reaction to food additive			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		

Investigations			
Blood calcium increased			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
White blood cell count increased			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Fall			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Procedural pain			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	4		
Skin laceration			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	8 / 55 (14.55%)		
occurrences (all)	8		
Loss of consciousness			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Memory impairment			

subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Neuralgia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	6 / 55 (10.91%)		
occurrences (all)	6		
Abdominal pain			
subjects affected / exposed	6 / 55 (10.91%)		
occurrences (all)	6		
Abdominal pain lower			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	7 / 55 (12.73%)		
occurrences (all)	7		
Constipation			
subjects affected / exposed	8 / 55 (14.55%)		
occurrences (all)	8		
Diarrhoea			
subjects affected / exposed	22 / 55 (40.00%)		
occurrences (all)	22		
Diverticulum			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Dry mouth			

subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Faeces discoloured			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Frequent bowel movements			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	18 / 55 (32.73%)		
occurrences (all)	18		
Varices oesophageal			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	5 / 55 (9.09%)		
occurrences (all)	5		
Hepatobiliary disorders			
Portal hypertension			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Photosensitivity reaction			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	6 / 55 (10.91%)		
occurrences (all)	6		
Rash			

subjects affected / exposed	5 / 55 (9.09%)		
occurrences (all)	5		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Nephrolithiasis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Proteinuria			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 55 (12.73%)		
occurrences (all)	7		
Back pain			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Flank pain			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Muscular weakness			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Musculoskeletal pain			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Neck pain			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Osteoarthritis			

subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Infections and infestations			
COVID-19			
subjects affected / exposed	13 / 55 (23.64%)		
occurrences (all)	13		
Lower respiratory tract infection			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Skin bacterial infection			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	4 / 55 (7.27%)		
occurrences (all)	4		
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Diabetes mellitus			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Increased appetite			
subjects affected / exposed	8 / 55 (14.55%)		
occurrences (all)	8		
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2019	The changes implemented with this amendment are: - to provide clarifications and details on how liver biopsy will be performed; - to clarify when statin use will commence for participating subjects.
29 January 2020	The changes implemented with this amendment are: - to primarily provide clarifications on lipid lowering algorithm; - to correct description of how subjects will be provided rosuvastatin upon LDL-C testing, i.e., appropriate doses will be shipped to subjects via a courier service instead of being picked up by the subjects on the study visit; - to correct description of how independent adjudication for adverse events of interest will be conducted; - to adjust certain criteria for selection of subjects.
24 September 2020	The changes implemented with this amendment are: - to update the NASH cirrhosis diagnosis based on recent guidelines; - to refine the population with respect to platelet count; - to include updates included in country-specific protocol amendments based on health authority feedback.
16 March 2021	The changes implemented with this amendment are: - to discontinue randomization of subjects to the aldafermin 0.3 mg dose level; - remove the total liver fat content requirement as measured by MRI-PDFF; - clarify inclusion criterion #4; - move FibroScan® from Day -42 to Day -56; - update exclusion #10 from total bilirubin within ULN to ≤1.3 mg/dL; - update EGD requirements to include application of the Baveno VI criteria (to no more than 30% of the remaining population); - allow non-statin lipid lowering agents until Day 1 of Screening (rather than 3 months); - allowed an increased screening window with Medical Monitor approval.
11 November 2021	The changes implemented with this amendment are: - to change the primary efficacy endpoint from histologic response in NASH CRN fibrosis score to change in ELF score based on recent literature supporting correlation of ELF with clinical outcomes and consistent with FDA Guidance on NASH with compensated cirrhosis (FDA 2019); - to clarify eligibility criteria; - to update statistical methods to account for the change in primary efficacy endpoint; - to make editorial and typographical changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported