Clinical trial results:
A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Explore the Efficacy and Safety of BIO89-100 in Subjects With Severe Hypertriglyceridemia

Summary

EudraCT number	2020-000641-13
Trial protocol	HU CZ PL
Global end of trial date	31 March 2023

Results information

Result version number	v1 (current)
This version publication date	28 December 2024
First version publication date	28 December 2024

Trial information

Trial identification

Sponsor protocol code	BIO89-100-221

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04541186
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	89bio, Inc.
Sponsor organisation address	655 Montgomery Street, Suite 1500, San Francisco, CA, United States, 94111
Public contact	Entrigue Study Team, 89bio, Inc., 1 4154329270, Ct.gov_SHTG@89bio.com
Scientific contact	Entrigue Study Team , 89bio, Inc., 1 4154329270, Ct.gov_SHTG@89bio.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	18 January 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 May 2022
Global end of trial reached?	Yes
Global end of trial date	31 March 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was designed to assess the efficacy, safety, and tolerability of different doses and dose regimens (once weekly [QW] or every 2 weeks [Q2W]), subcutaneous (SC) dosing of BIO89-100 (pegozafermin) compared to placebo in participants with severe hypertriglyceridemia (SHTG).

Protection of trial subjects:

This study was conducted according to the ethical principles derived from the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines, International Council for Harmonisation (ICH) guidelines for Good Clinical Practice (GCP), and applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2020
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	United States: 58
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	Poland: 14
Country: Number of subjects enrolled	Czechia: 4
Worldwide total number of subjects	86
EEA total number of subjects	28

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)	70
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants in the Main Study cohort were randomized in a 1:1:1:1:1 ratio to 1 of 4 doses of pegozafermin (9 mg QW, 18 mg QW, 27 mg QW, or 36 mg Q2W) or matching placebo. Participants in the Fibrate Expansion cohort were randomized in a 1:1 ratio to pegozafermin 27 mg QW or matching placebo.

Pre-assignment

Screening details:

Four participants randomized to 9 mg received 18 mg instead. One participant was randomized but did not receive treatment. Full Analysis set analyzed participants as per randomized assignment. Safety Analysis set analyzed participants as per treatment received.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pegozafermin 9 mg QW

Arm description:

Pegozafermin 9 mg QW was administered as a SC injection.

Arm type	Experimental
Investigational medicinal product name	Pegozafermin
Investigational medicinal product code	
Other name	BIO89-100
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received pegozafermin 9 mg QW as an SC injection for 8 weeks in the Main Study cohort.

Arm title	Pegozafermin 18 mg QW

Arm description:

Pegozafermin 18 mg QW was administered as an SC injection.

Arm type	Experimental
Investigational medicinal product name	Pegozafermin
Investigational medicinal product code	
Other name	BIO89-100
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received pegozafermin 18 mg QW as an SC injection for 8 weeks in the Main Study cohort.

Arm title	Pegozafermin 27 mg QW

Arm description:

Pegozafermin 27 mg QW was administered as an SC injection. The Main Study cohort and Fibrate Expansion cohorts for pegozafermin 27 mg were pooled together due to low sample size in the expansion cohort.

Arm type	Experimental

Investigational medicinal product name	Pegozafermin
Investigational medicinal product code	
Other name	BIO89-100
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received pegozafermin 27 QW as an SC injection for 8 weeks in the Main Study cohort or Fibrate Expansion cohort.

Arm title	Pegozafermin 36 mg Q2W

Arm description:

Pegozafermin 36 mg Q2W was administered as an SC injection.

Arm type	Experimental
Investigational medicinal product name	Pegozafermin
Investigational medicinal product code	
Other name	BIO89-100
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received pegozafermin 36 mg Q2W as an SC injection for 8 weeks in the Main Study cohort.

Arm title	Placebo

Arm description:

Matching placebo was injected at matching frequency per assigned cohort. The Main Study cohort and Fibrate Expansion cohorts for placebo were pooled together due to low sample size in the expansion cohort.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching placebo was injected at matching frequency per assigned cohort for 8 weeks in the Main Study cohort or Fibrate Expansion cohort.

Number of subjects in period 1	Pegozafermin 9 mg QW	Pegozafermin 18 mg QW	Pegozafermin 27 mg QW
Started	16	17	19
Full Analysis Set (FAS)	16	17	16
Received at Least 1 Dose of Study Drug	16	17	18
Completed	15	16	13
Not completed	1	1	6
Consent withdrawn by subject	1	1	-
Adverse event, non-fatal	-	-	4
COVID-19-related Dose Interruption	-	-	-
Randomized in Error Not Treated	-	-	1
Other than Specified	-	-	-
Investigator Decision	-	-	1

Number of subjects in period 1	Pegozafermin 36 mg Q2W	Placebo
Started	16	18
Full Analysis Set (FAS)	16	17
Received at Least 1 Dose of Study Drug	16	18
Completed	15	16
Not completed	1	2
Consent withdrawn by subject	-	-
Adverse event, non-fatal	-	-
COVID-19-related Dose Interruption	-	1
Randomized in Error Not Treated	-	-
Other than Specified	-	1
Investigator Decision	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Pegozafermin 9 mg QW
Reporting group description:	
Pegozafermin 9 mg QW was administered as a SC injection.	
Reporting group title	Pegozafermin 18 mg QW
Reporting group description:	
Pegozafermin 18 mg QW was administered as an SC injection.	
Reporting group title	Pegozafermin 27 mg QW
Reporting group description:	
Pegozafermin 27 mg QW was administered as an SC injection. The Main Study cohort and Fibrate Expansion cohorts for pegozafermin 27 mg were pooled together due to low sample size in the expansion cohort.	
Reporting group title	Pegozafermin 36 mg Q2W
Reporting group description:	
Pegozafermin 36 mg Q2W was administered as an SC injection.	
Reporting group title	Placebo
Reporting group description:	
Matching placebo was injected at matching frequency per assigned cohort. The Main Study cohort and Fibrate Expansion cohorts for placebo were pooled together due to low sample size in the expansion cohort.	

Reporting group values	Pegozafermin 9 mg QW	Pegozafermin 18 mg QW	Pegozafermin 27 mg QW
Number of subjects	16	17	19
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: years			
arithmetic mean	54.6	49.2	54.5
standard deviation	± 12.71	± 10.85	± 7.43
Sex: Female, Male Units: participants			
Female	5	3	5
Male	11	14	14

Reporting group values	Pegozafermin 36 mg Q2W	Placebo	Total
Number of subjects	16	18	86

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)			0
From 65-84 years			0
85 years and over			0
Age Continuous Units: years			
arithmetic mean	53.1	57.5	
standard deviation	± 12.36	± 10.30	-
Sex: Female, Male Units: participants			
Female	2	6	21
Male	14	12	65

End points

End points reporting groups

Reporting group title	Pegozafermin 9 mg QW
Reporting group description:	
Pegozafermin 9 mg QW was administered as a SC injection.	
Reporting group title	Pegozafermin 18 mg QW
Reporting group description:	
Pegozafermin 18 mg QW was administered as an SC injection.	
Reporting group title	Pegozafermin 27 mg QW
Reporting group description:	
Pegozafermin 27 mg QW was administered as an SC injection. The Main Study cohort and Fibrate Expansion cohorts for pegozafermin 27 mg were pooled together due to low sample size in the expansion cohort.	
Reporting group title	Pegozafermin 36 mg Q2W
Reporting group description:	
Pegozafermin 36 mg Q2W was administered as an SC injection.	
Reporting group title	Placebo
Reporting group description:	
Matching placebo was injected at matching frequency per assigned cohort. The Main Study cohort and Fibrate Expansion cohorts for placebo were pooled together due to low sample size in the expansion cohort.	
Subject analysis set title	Pegozafermin
Subject analysis set type	Full analysis
Subject analysis set description:	
FAS: All randomized participants who received at least 1 dose of study drug, had a baseline and at least 1 post-baseline triglyceride (TG) measurement not including end of study (EOS) visit. Main study and fibrate expansion cohorts were combined due to the low number of participants in fibrate expansion cohort. All dose groups for pegozafermin were pooled to evaluate the overall effectiveness of pegozafermin. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
FAS: All randomized participants who received at least 1 dose of study drug, had a baseline and at least 1 post-baseline TG measurement not including EOS visit. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure. Main study and fibrate expansion cohorts were combined due to the low number of participants in fibrate expansion cohort. All dose groups for placebo groups were pooled.	
Subject analysis set title	Pegozafermin 9 mg QW (Safety)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Pegozafermin 9 mg QW was administered as an SC injection. Participants were summarized by treatment received.	
Subject analysis set title	Pegozafermin 18 mg QW (Safety)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Pegozafermin 18 mg QW was administered as an SC injection. Participants were summarized by treatment received.	
Subject analysis set title	Pegozafermin 27 mg QW (Safety)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Pegozafermin 27 mg QW was administered as an SC injection. Participants were summarized by treatment received. The Main Study cohort and Fibrate Expansion cohort for pegozafermin 27 mg were pooled together due to low sample size in the expansion cohort.	

Subject analysis set title	Pegozafermin 36 mg Q2W (Safety)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Pegozafermin 36 mg Q2W was administered as an SC injection. Participants were summarized by treatment received.	
Subject analysis set title	Placebo (Safety)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Placebo was administered as an SC injection. Participants were summarized by treatment received. The Main Study cohort and Fibrate Expansion cohort for placebo were pooled together due to low sample size in the expansion cohort.	

Primary: Percent Change from Baseline to Week 8 in Serum TG

End point title	Percent Change from Baseline to Week 8 in Serum TG
End point description:	
FAS: All randomized participants who received at least 1 dose of study drug, had a baseline and at least 1 post-baseline TG measurement not including EOS visit. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure. As pre-specified in the SAP, the sample size in each arm (by dose group) was insufficient (under powered) to effectively evaluate differences in efficacy by dose, therefore, efficacy analysis was performed using total pegozafermin and placebo groups.	
End point type	Primary
End point timeframe:	
Baseline, Week 8	

End point values	Pegozafermin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64	17		
Units: percent change from Baseline				
median (inter-quartile range (Q1-Q3))	-57.33 (-69.07 to -32.31)	-11.85 (-23.22 to 7.88)		

Statistical analyses

Statistical analysis title	Percent Change From Baseline to Week 8 in Serum TG
Comparison groups	Pegozafermin v Placebo
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.001 [2]
Method	van Elteren test
Parameter estimate	Median Percent Change Difference
Point estimate	-43.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-57.08
upper limit	-30.31

Notes:

[1] - Nonparametric analysis stratified by baseline TG level and background lipid therapy to test the treatment difference using pooled data.
The location shift and Hodges-Lehmann 95% confidence interval were based on Hodges-Lehman estimation. Placebo group is the reference group, and the comparison was performed in pooled pegozafermin treatment group vs. placebo pooled.
[2] - Significant level = 0.05

Secondary: Percentage of Participants Who Achieved TG Level <500 mg/dL at Week 8

End point title	Percentage of Participants Who Achieved TG Level <500 mg/dL at Week 8

End point description:

FAS: All randomized participants who received at least 1 dose of study drug, had a baseline and at least 1 post-baseline TG measurement not including EOS visit. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure. As pre-specified in the SAP, the sample size in each arm (by dose group) was insufficient (under powered) to effectively evaluate differences in efficacy by dose, therefore, efficacy analysis was performed using total pegozafermin and placebo groups.

End point type	Secondary

End point timeframe:

Week 8

End point values	Pegozafermin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64	17		
Units: percentage				
number (not applicable)	79.69	29.41		

Statistical analyses

Statistical analysis title	Achieved TG Level <500 mg/dL at Week 8

Statistical analysis description:

Cochran-Mantel-Haenszel test stratified by baseline TG level and lipid modifying therapy use.

Comparison groups	Placebo v Pegozafermin
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	Cochran-Mantel-Haenszel

Notes:

[3] - Significant level = 0.05

Secondary: Percent Change From Baseline to Week 8 in Non-high-density Lipoprotein Cholesterol (Non-HDL-C), Apolipoprotein B100 (ApoB), Low-density Lipoprotein Cholesterol (LDL-C), and High-density Lipoprotein Cholesterol (HDL-C)

End point title	Percent Change From Baseline to Week 8 in Non-high-density Lipoprotein Cholesterol (Non-HDL-C), Apolipoprotein B100 (ApoB), Low-density Lipoprotein Cholesterol (LDL-C), and High-density Lipoprotein Cholesterol (HDL-C)

End point description:

Least Squares Mean was calculated using Mixed model with repeated measure (MMRM).
FAS: All randomized participants who received at least 1 dose of study drug, had a baseline and at least 1 post-baseline TG measurement not including EOS visit. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure. As pre-specified in the SAP, the sample size in each arm (by dose group) was insufficient (under powered) to effectively evaluate differences in efficacy by dose, therefore, efficacy analysis was performed using total pegozafermin and placebo groups.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Pegozafermin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	17		
Units: percent change				
least squares mean (standard error)				
Non-HDL-C (n=63 and 17)	-18.29 (± 2.943)	-0.57 (± 5.586)		
ApoB (n=63 and 17)	-10.51 (± 2.238)	1.07 (± 4.309)		
LDL-C (n=62 and 15)	10.44 (± 4.654)	8.72 (± 9.018)		
HDL-C (n=63 and 17)	24.65 (± 3.752)	9.67 (± 7.045)		

Statistical analyses

Statistical analysis title	Percent Change From Baseline to Week 8: non-HDL-C

Statistical analysis description:

MMRM analysis of non-HDL-C comparison between pegozafermin pooled versus placebo pooled group.

Comparison groups	Pegozafermin v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007 [4]
Method	MMRM
Parameter estimate	Least Squares Means Difference
Point estimate	-17.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.67
upper limit	-5.07
Variability estimate	Standard error of the mean
Dispersion value	6.425

Notes:

[4] - Significant level = 0.05

Statistical analysis title	Percent Change From Baseline to Week 8 in ApoB
Statistical analysis description:	
MMRM analysis of ApoB comparison between pegozafermin pooled versus placebo pooled group.	
Comparison groups	Pegozafermin v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019 [5]
Method	MMRM
Parameter estimate	Least Squares Means Difference
Point estimate	-11.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.48
upper limit	-2.01
Variability estimate	Standard error of the mean
Dispersion value	4.888

Notes:

[5] - Significant level of 0.05

Statistical analysis title	Percent Change From Baseline to Week 8 in LDL-C
Statistical analysis description:	
MMRM analysis of LDL-C comparison between pegozafermin pooled versus placebo pooled group.	
Comparison groups	Pegozafermin v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.87 [6]
Method	MMRM
Parameter estimate	Least Squares Means Difference
Point estimate	1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.21
upper limit	22.68
Variability estimate	Standard error of the mean
Dispersion value	10.519

Notes:

[6] - Significant level of 0.05

Statistical analysis title	Percent Change From Baseline to Week 8 in HDL-C
Statistical analysis description:	
MMRM analysis of HDL-C comparison between pegozafermin pooled versus placebo pooled group.	
Comparison groups	Pegozafermin v Placebo

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.064 [7]
Method	MMRM
Parameter estimate	Least Squares Means Difference
Point estimate	15.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	31.7
Variability estimate	Standard error of the mean
Dispersion value	8.182

Notes:

[7] - Significant level of 0.05

Secondary: Percent Change From Baseline to Week 8 in Very Low-density Lipoprotein Cholesterol (VLDL-C) and VLDL-TG

End point title	Percent Change From Baseline to Week 8 in Very Low-density Lipoprotein Cholesterol (VLDL-C) and VLDL-TG

End point description:

FAS: All randomized participants who received at least 1 dose of study drug, had a baseline and at least 1 post-baseline TG measurement not including EOS visit. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure. As pre-specified in the SAP, the sample size in each arm (by dose group) was insufficient (under powered) to effectively evaluate differences in efficacy by dose, therefore, efficacy analysis was performed using total pegozafermin and placebo groups.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Pegozafermin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	62	15		
Units: percent change				
median (inter-quartile range (Q1-Q3))				
VLDC-C (n=62 and 15)	-47.96 (-63.14 to -16.67)	-0.41 (-30.38 to 10.98)		
VLDL-TG (n= 61 and 15)	-58.50 (-72.53 to -32.80)	-0.85 (-27.72 to 14.25)		

Statistical analyses

Statistical analysis title	Percent Change From Baseline to Week 8 in VLDL-TG

Statistical analysis description:

Nonparametric analysis of VLDL-TG comparison between pegozafermin pooled versus placebo pooled group.

Comparison groups	Pegozafermin v Placebo

Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [8]
Method	van Elteren Test

Notes:

[8] - Significant level of 0.05

Statistical analysis title	Percent Change From Baseline to Week 8 in VLDL-C

Statistical analysis description:

Nonparametric analysis of VLDL-C comparison between pegozafermin pooled versus placebo pooled group.

Comparison groups	Pegozafermin v Placebo
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 [9]
Method	van Elteren Test

Notes:

[9] - Significant level of 0.05

Secondary: Percent Change in Baseline to Week 8 in Fasting Plasma Glucose, Adiponectin, and Body Weight

End point title	Percent Change in Baseline to Week 8 in Fasting Plasma Glucose, Adiponectin, and Body Weight

End point description:

Least Squares Mean was calculated using MMRM.
FAS: All randomized participants who received at least 1 dose of study drug, had a baseline and at least 1 post-baseline TG measurement not including EOS visit. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure. As pre-specified in the SAP, the sample size in each arm (by dose group) was insufficient (under powered) to effectively evaluate differences in efficacy by dose, therefore, efficacy analysis was performed using total pegozafermin and placebo groups.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Pegozafermin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	17		
Units: percent change				
least squares mean (standard error)				
Fasting Plasma Glucose	-3.90 (± 2.681)	-2.67 (± 5.230)		
Adiponectin	69.53 (± 7.383)	5.70 (± 14.556)		
Body Weight	-0.15 (± 0.339)	-0.14 (± 0.654)		

Statistical analyses

Statistical analysis title	Percent Change in Fasting Plasma Glucose

Statistical analysis description:

MMRM analysis of the percent change in Baseline to Week 8 in fasting plasma glucose comparison between pegozafermin pooled versus placebo pooled group.

Comparison groups	Pegozafermin v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.809 [10]
Method	MMRM

Notes:

[10] - Significant level = 0.05

Statistical analysis title	Percent Change in Adiponectin

Statistical analysis description:

MMRM analysis of the percent change in Baseline to Week 8 in adiponectin comparison between pegozafermin pooled versus placebo pooled group.

Comparison groups	Pegozafermin v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [11]
Method	MMRM

Notes:

[11] - Significant level = 0.05

Statistical analysis title	Percent Change in Body Weight

Statistical analysis description:

MMRM analysis of the percent change in Baseline to Week 8 in body weight comparison between pegozafermin pooled versus placebo pooled group.

Comparison groups	Pegozafermin v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.973 [12]
Method	MMRM

Notes:

[12] - Significant level = 0.05

Secondary: Percent Change From Baseline to Week 8 in High-sensitivity C-reactive Protein (hsCRP)

End point title	Percent Change From Baseline to Week 8 in High-sensitivity C-reactive Protein (hsCRP)

End point description:

FAS: All randomized participants who received at least 1 dose of study drug, had a baseline and at least

1 post-baseline TG measurement not including EOS visit. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure. As pre-specified in the SAP, the sample size in each arm (by dose group) was insufficient (under powered) to effectively evaluate differences in efficacy by dose, therefore, efficacy analysis was performed using total pegozafermin and placebo groups.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Pegozafermin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	17		
Units: percent change				
median (inter-quartile range (Q1-Q3))	-21.43 (-43.30 to 42.37)	-1.10 (-50.41 to 18.84)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Week 8 in Liver Fat as Assessed by Magnetic Resonance Imaging - Whole Liver Proton Density Fat Fraction (MRI-PDFF)

End point title	Percent Change From Baseline to Week 8 in Liver Fat as Assessed by Magnetic Resonance Imaging - Whole Liver Proton Density Fat Fraction (MRI-PDFF)

End point description:

Least Squares Mean was calculated using analysis of covariance (ANCOVA).
FAS: All randomized participants who received at least 1 dose of study drug, had a baseline and at least 1 post-baseline TG measurement not including EOS visit. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure. As pre-specified in the SAP, the sample size in each arm (by dose group) was insufficient (under powered) to effectively evaluate differences in efficacy by dose, therefore, efficacy analysis was performed using total pegozafermin and placebo groups.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Pegozafermin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	6		
Units: percent change				
least squares mean (standard error)	-42.18 (± 6.207)	-8.26 (± 11.214)		

Statistical analyses

Statistical analysis title	Percent Change From Baseline to Week 8: Liver Fat
Comparison groups	Pegozafermin v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012 [13]
Method	ANCOVA

Notes:

[13] - Significant level = 0.05

Secondary: Percent Change From Baseline to Week 8 in Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST)

End point title	Percent Change From Baseline to Week 8 in Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST)

End point description:

Least Squares Mean was calculated using MMRM.
FAS: All randomized participants who received at least 1 dose of study drug, had a baseline and at least 1 post-baseline TG measurement not including EOS visit. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure. As pre-specified in the SAP, the sample size in each arm (by dose group) was insufficient (under powered) to effectively evaluate differences in efficacy by dose, therefore, efficacy analysis was performed using total pegozafermin and placebo groups.

End point type	Secondary

End point timeframe:

Baseline, Week 8

End point values	Pegozafermin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	17		
Units: percent change				
least squares mean (standard error)				
ALT	-4.28 (± 4.549)	0.43 (± 8.881)		
AST	-11.50 (± 3.341)	0.51 (± 6.597)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 (after dosing) up to 12 weeks

Adverse event reporting additional description:

As per SAP, participants in the pegozafermin 27 mg QW fibrate cohort were pooled with the pegozafermin 27 mg QW main cohort. Similarly, placebo groups in main and fibrate cohorts were pooled.
Safety data analysis was by treatment group received. 4 participants randomized to receive 9 mg QW received 18 mg QW instead.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Pegozafermin 9 mg QW (Safety)

Reporting group description:

Pegozafermin 9 mg QW was administered as a SC injection.
Participants were summarized by treatment received.

Reporting group title	Pegozafermin 18 mg QW (Safety)

Reporting group description:

Pegozafermin 18 mg QW was administered as an SC injection.
Participants were summarized by treatment received.

Reporting group title	Placebo (Safety)

Reporting group description:

Matching placebo was injected at matching frequency per assigned cohort.
Participants were summarized by treatment received.
Main Study cohort and Fibrate Expansion cohort for placebo were pooled together due to low sample size in the expansion cohort.

Reporting group title	Pegozafermin 36 mg Q2W (Safety)

Reporting group description:

Pegozafermin 36 mg Q2W was administered as an SC injection.
Participants were summarized by treatment received.

Reporting group title	Pegozafermin 27 mg QW (Safety)

Reporting group description:

Pegozafermin 27 mg QW was administered as an SC injection. The Main Study cohort and Fibrate Expansion cohort for pegozafermin 27 mg were pooled together due to low sample size in the expansion cohort.

Serious adverse events	Pegozafermin 9 mg QW (Safety)	Pegozafermin 18 mg QW (Safety)	Placebo (Safety)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			

subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Pegozafermin 36 mg Q2W (Safety)	Pegozafermin 27 mg QW (Safety)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pegozafermin 9 mg QW (Safety)	Pegozafermin 18 mg QW (Safety)	Placebo (Safety)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	13 / 21 (61.90%)	9 / 18 (50.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 21 (4.76%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Injection site reaction			
subjects affected / exposed	1 / 12 (8.33%)	2 / 21 (9.52%)	0 / 18 (0.00%)
occurrences (all)	1	3	0
Injection site pruritus			

subjects affected / exposed	1 / 12 (8.33%)	2 / 21 (9.52%)	0 / 18 (0.00%)
occurrences (all)	1	3	0
Injection site pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Injection site induration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	1 / 12 (8.33%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 12 (0.00%)	1 / 21 (4.76%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
C-reactive protein increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Injury, poisoning and procedural			

complications			
Skin laceration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Foot fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Corneal abrasion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Taste disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Lymphadenitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 12 (8.33%)	1 / 21 (4.76%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Diverticulum			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	2 / 12 (16.67%)	1 / 21 (4.76%)	1 / 18 (5.56%)
occurrences (all)	2	1	1
Frequent bowel movements			
subjects affected / exposed	0 / 12 (0.00%)	1 / 21 (4.76%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			

Hepatic steatosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pigmentation disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 12 (0.00%)	3 / 21 (14.29%)	3 / 18 (16.67%)
occurrences (all)	0	3	3
Respiratory tract infection viral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Otitis media			

subjects affected / exposed	0 / 12 (0.00%)	1 / 21 (4.76%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 12 (0.00%)	1 / 21 (4.76%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Hypomagnesaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 21 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Pegozafermin 36 mg Q2W (Safety)	Pegozafermin 27 mg QW (Safety)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 16 (43.75%)	13 / 18 (72.22%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Lymphoedema			

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	1 / 16 (6.25%)	2 / 18 (11.11%)	
occurrences (all)	3	10	
Injection site reaction			
subjects affected / exposed	2 / 16 (12.50%)	1 / 18 (5.56%)	
occurrences (all)	2	2	
Injection site pruritus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	2	
Injection site pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Injection site induration			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Injection site bruising			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Wheezing			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Investigations			

Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
C-reactive protein increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Foot fracture			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Corneal abrasion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Contusion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Supraventricular extrasystoles			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Taste disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Dysgeusia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Iron deficiency anaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Lymphadenitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	2 / 16 (12.50%)	5 / 18 (27.78%)	
occurrences (all)	2	8	
Diverticulum			

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	1 / 16 (6.25%)	2 / 18 (11.11%)	
occurrences (all)	3	3	
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	4 / 18 (22.22%)	
occurrences (all)	0	4	
Frequent bowel movements			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Ecchymosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Pigmentation disorder			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	0 / 16 (0.00%)	2 / 18 (11.11%)	
occurrences (all)	0	2	

Pain in extremity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Otitis media			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Sinusitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Hypoglycaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Increased appetite			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Hypomagnesaemia			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 18 (5.56%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 May 2020	- Specific laboratory assessments were added or amended. - Updated eligibility criteria - Added stopping role of "External circumstances that do not enable the study to be properly conducted under the existing protocol. - Clarified that only central labs and protocol defined assessments may be used for screening and at baseline.
23 December 2020	- Updated study population - Expanded description of re-screening - Updated secondary endpoints - Clarified clinical laboratory assessments - Risk assessment section updated based on currently available data - Updated eligibility criteria
03 May 2021	- Updated clinical laboratory assessments - Updated eligibility criteria

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study did not separately evaluate the response to pegozafermin in participants who were on and who were not on concurrent fibrate therapy due to small sample size in the Fibrate Expansion cohort.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/37355760