Clinical trial results:
Trial of Pamrevlumab (FG-3019), a Monoclonal Antibody to Connective Tissue Growth Factor, in Non-Ambulatory Subjects With Duchenne Muscular Dystrophy

Summary

EudraCT number	2023-000321-80
Trial protocol	Outside EU/EEA
Global end of trial date	07 August 2023

Results information

Result version number	v1
This version publication date	22 February 2024
First version publication date	22 February 2024

Trial information

Trial identification

Sponsor protocol code	FGCL-3019-079

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02606136
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	FibroGen, Inc.
Sponsor organisation address	409 Illinois Street, San Francisco, United States, CA 94158
Public contact	Clinical Trial Information Desk, FibroGen, Inc., FG3019-079DMDStudy@fibrogen.com
Scientific contact	Clinical Trial Information Desk, FibroGen, Inc., FG3019-079DMDStudy@fibrogen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002979-PIP01-21
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?	Yes

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	07 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 May 2020
Global end of trial reached?	Yes
Global end of trial date	07 August 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial is to estimate pamrevlumab’s efficacy in non-ambulatory participants with Duchenne Muscular Dystrophy (DMD).

Protection of trial subjects:

The study was conducted and monitored in accordance with United States (US) Food and Drug Administration (FDA) regulations, the International Council for Harmonisation E6 Guideline for Good Clinical Practice (GCP), the Declaration of Helsinki, any other applicable regulatory requirements, and Institutional Review Board (IRB) requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 January 2016
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: 21
Worldwide total number of subjects	21
EEA total number of subjects	0

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)	19
Adults (18-64 years)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All participants who completed the main portion of the study for a minimum of 104 weeks (2 years) were rolled over to an open-label extension (OLE) for up to an additional 208 weeks (4 years). Some participants remained in the main study for up to 206 weeks before rolling over to the OLE.

Pre-assignment

Screening details:

The last Week 104 visit for the primary endpoint occurred on 07 May 2020.

Period 1

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

Arms

Arm title	Pamrevlumab

Arm description:

Participants received pamrevlumab 35 milligrams (mg)/kilogram (kg) by intravenous (IV) infusion every 2 weeks for a minimum of 104 weeks.

Arm type	Experimental
Investigational medicinal product name	Pamrevlumab
Investigational medicinal product code	
Other name	Monoclonal Antibody to Connective tissue growth factor (CTGF), FG-3019
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pamrevlumab was administered per dose and schedule specified in the arm description.

Number of subjects in period 1	Pamrevlumab
Started	21
Received at Least 1 Dose of Study Drug	21
Completed	15
Not completed	6
Consent withdrawn by subject	1
Participant/Legal Guardian Decision	5

Baseline characteristics

Reporting groups	
Reporting group title	Pamrevlumab
Reporting group description:	
Participants received pamrevlumab 35 milligrams (mg)/kilogram (kg) by intravenous (IV) infusion every 2 weeks for a minimum of 104 weeks.	

Reporting group values	Pamrevlumab	Total	
Number of subjects	21	21	
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	15.99		
standard deviation	± 3.277	-	
Sex: Female, Male Units: participants			
Female	0	0	
Male	21	21	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	1	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	20	20	
More than one race	0	0	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	2	
Not Hispanic or Latino	19	19	
Unknown or Not Reported	0	0	
Percent Predicted Forced Vital Capacity (ppFVC)			
FVC is a standard pulmonary function test used to quantify respiratory muscle weakness. FVC was the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. Predicted FVC is based on a formula using sex, age and height of a person, and is an estimate of healthy lung capacity. Percent of predicted FVC = (observed value)/(predicted value) * 100%.			
Units: percentage of predicted FVC			
arithmetic mean	54.15		
full range (min-max)	29.1 to 70.7	-	
Left Ventricular Ejection Fraction Percentage (LVEF%)			
LVEF% is an important measure of cardiac function. LVEF is a fraction of blood (in percent) pumped out of the left ventricle of the heart (the main pumping chamber).			
Units: percentage of LVEF			
arithmetic mean	56.992		

full range (min-max)	41.03 to 73.81	-	
Percent Predicted Forced Expiratory Volume at 1 Second (ppFEV1)			
FEV1 is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation. Predicted FEV1 is based on a formula using sex, age and height of a person, and is an estimate of healthy lung capacity. Percent of predicted FEV1= (observed value)/(predicted value) * 100%.			
Units: percentage of predicted FEV1			
arithmetic mean	53.815		
full range (min-max)	29.24 to 73.35	-	
Percent Predicted Peak Expiratory Flow (PEF)			
Percent predicted PEF is a measure of the maximal or peak flow produced during an exhalation with maximal effort and, as such, is the most effortdependent measure of lung function.			
Units: percentage of predicted PEF			
arithmetic mean	54.66		
full range (min-max)	37.9 to 82.7	-	
Grip Strength by Hand (Dominant Grip Best Result), as Measured by HHM			
The HHM was used to measure distal upper arm strength (grip strength).			
Units: newton			
arithmetic mean	45.861		
full range (min-max)	3 to 142.2	-	
Cardiac Fibrosis Score (Scar Mass), as Measured by Magnetic Resonance Imaging (MRI)			
'Number of participants analyzed' = 20			
Units: grams			
arithmetic mean	24.100		
full range (min-max)	0.44 to 76.09	-	
Upper Arm (Biceps Brachii MRI) Muscle Fat and Fibrosis Score			
T2-mapping with MRI was conducted to measure upper arm muscle fibrosis and fat in the biceps brachii muscle. 'Number of participants analyzed' = 12			
Units: unit on a scale			
arithmetic mean	8.01		
full range (min-max)	3.9 to 17.2	-	
Fat Fraction Percentage (%F), as Measured by MRI			
'Number of participants analyzed' = 9			
Units: percentage of fat			
arithmetic mean	22.07		
full range (min-max)	4 to 32.6	-	
Pinch Strength (Non-Dominant Pinch Best Result), as Measured by Hand Held Myometry (HHM)			
The HHM was used to measure distal upper arm strength (pinch strength).			
Units: newton			
arithmetic mean	16.607		
full range (min-max)	0 to 47.1	-	
Grip Strength by Hand, as Measured by HHM			
The HHM was used to measure distal upper arm strength (grip strength). Data has been presented by dominant and non-dominant hand.			
Units: newton			
arithmetic mean	45.861		
full range (min-max)	3 to 142.2	-	

Grip Strength by Hand (Non-Dominant Grip Best Result), as Measured by HHM			
The HHM was used to measure distal upper arm strength (grip strength).			
Units: newton			
arithmetic mean	41.977		
full range (min-max)	2 to 104.9	-	
Pinch Strength (Dominant Pinch Best Result), as Measured by Hand Held Myometry (HHM)			
The HHM was used to measure distal upper arm strength (pinch strength).			
Units: newton			
arithmetic mean	17.003		
full range (min-max)	0 to 45.1	-	
Performance of Upper Limb (PUL) Total Score			
PUL scale includes 22 items; an entry item defining starting functional level, and 21 items subdivided into shoulder level (4 items), elbow level (9 items), and distal level (8 items) dimensions. Scoring options per item may vary from 0-1 and 0-6, according to performance, with higher values indicating better performance. Each dimension was scored separately with a maximum score of 16 for shoulder level, 34 for elbow level, and 24 for distal level. Total score was calculated by adding 3 level scores, with a maximum global score of 74 (total score range = 0-74). Higher score = better outcome.			
Units: unit on a scale			
arithmetic mean	24.4		
full range (min-max)	13 to 41	-	
Pinch Strength, as Measured by Hand Held Myometry (HHM)			
The HHM was used to measure distal upper arm strength (pinch strength). Data has been presented by dominant and non-dominant hand.			
Units: newton			
arithmetic mean	16.607		
full range (min-max)	0 to 47.1	-	

End points

End points reporting groups

Reporting group title	Pamrevlumab

Reporting group description:

Participants received pamrevlumab 35 milligrams (mg)/kilogram (kg) by intravenous (IV) infusion every 2 weeks for a minimum of 104 weeks.

Primary: Annual Change From Baseline in Percent Predicted Forced Vital Capacity (ppFVC) at Week 104

End point title	Annual Change From Baseline in Percent Predicted Forced Vital Capacity (ppFVC) at Week 104[1]

End point description:

FVC is a standard pulmonary function test used to quantify respiratory muscle weakness. FVC was the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. Predicted FVC is based on a formula using sex, age and height of a person, and is an estimate of healthy lung capacity. Percent of predicted FVC = (observed value)/(predicted value) * 100%. Analysis was done using a random coefficient model (RCM), which included visit in years (as a continuous variable), and baseline efficacy as fixed effects, the intercept and the linear slope of visit as random effect, and individual participants as participant effect. ITT population included all participants who enrolled in the study.

End point type	Primary

End point timeframe:

Baseline, Week 104

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: Statistical analysis was not planned for this endpoint.

End point values	Pamrevlumab			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: percentage of predicted FVC				
least squares mean (standard error)	-8.15 (± 1.079)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Percent Predicted Forced Expiratory Volume at 1 Second (ppFEV1) at Week 104

End point title	Change From Baseline in Percent Predicted Forced Expiratory Volume at 1 Second (ppFEV1) at Week 104

End point description:

FEV1 is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation. Predicted FEV1 is based on a formula using sex, age and height of a person, and is an estimate of healthy lung capacity. Percent of predicted FEV1= (observed value)/(predicted value) * 100%. Analysis was done using an RCM, which included visit in years (as a continuous variable), and baseline efficacy as fixed effects, the intercept and the linear slope of visit as random effect, and individual participants as participant effect. ITT population included all participants who enrolled in the

study.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Pamrevlumab			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: percentage of predicted FEV1				
least squares mean (standard error)	-8.32 (± 1.217)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Percent Predicted Peak Expiratory Flow (PEF) at Week 104

End point title	Change From Baseline in Percent Predicted Peak Expiratory Flow (PEF) at Week 104

End point description:

Percent predicted PEF is a measure of the maximal or peak flow produced during an exhalation with maximal effort and, as such, is the most effortdependent measure of lung function. Analysis was done using an RCM, which included visit in years (as a continuous variable), and baseline efficacy as fixed effects, the intercept and the linear slope of visit as random effect, and individual participants as participant effect. ITT population included all participants who enrolled in the study.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Pamrevlumab			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: percentage of predicted PEF				
least squares mean (standard error)	-7.13 (± 2.313)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Left Ventricular Ejection Fraction Percentage (LVEF%) at Week 104

End point title	Change From Baseline in Left Ventricular Ejection Fraction Percentage (LVEF%) at Week 104

End point description:

LVEF% is an important measure of cardiac function. LVEF is a fraction of blood (in percent) pumped out of the left ventricle of the heart (the main pumping chamber). Analysis was done using an RCM, which included visit in years (as a continuous variable), and baseline efficacy as fixed effects, the intercept and the linear slope of visit as random effect, and individual participants as participant effect. ITT population included all participants who enrolled in the study.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Pamrevlumab			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: percentage of LVEF				
least squares mean (standard error)	-2.73 (± 1.651)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Performance of Upper Limb (PUL) Total Score at Week 104

End point title	Change From Baseline in Performance of Upper Limb (PUL) Total Score at Week 104

End point description:

PUL was used to assess motor performance of upper limb. PUL scale includes 22 items; an entry item defining the starting functional level, and 21 items subdivided into shoulder level (4 items), elbow level (9 items), and distal level (8 items) dimensions. Scoring options per item may not be uniform and may vary from 0-1 and 0-6, according to performance, with higher values corresponding to better performance. Each dimension was scored separately with a maximum score of 16 for shoulder level, 34 for elbow level, and 24 for distal level. Total score was calculated by adding 3 level scores, with a maximum global score of 74 (total score range = 0-74). Higher score = better outcome. Analysis was done using an RCM, which included visit in years (as a continuous variable), and baseline efficacy as fixed effects, the intercept and the linear slope of visit as random effect, and individual participants as participant effect. ITT population included all participants who enrolled in the study.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Pamrevlumab			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: unit on a scale				
least squares mean (standard error)	-4.14 (± 0.651)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pinch Strength, as Measured by HHM at Week 104

End point title	Change From Baseline in Pinch Strength, as Measured by HHM at Week 104

End point description:

The HHM was used to measure distal upper arm strength (pinch strength). Data has been presented by dominant and non-dominant hand. Analysis was done using an RCM, which included visit in years (as a continuous variable), and baseline efficacy as fixed effects, the intercept and the linear slope of visit as random effect, and individual participants as participant effect. ITT population included all participants who enrolled in the study.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Pamrevlumab			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: newton				
least squares mean (standard error)				
Dominant Pinch Best Result	-4.24 (± 1.547)			
Non-Dominant Pinch Best Result	-3.46 (± 1.378)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Grip Strength by Hand, as Measured by Hand Held Myometry (HHM) at Week 104

End point title	Change From Baseline in Grip Strength by Hand, as Measured by Hand Held Myometry (HHM) at Week 104

End point description:

The HHM was used to measure distal upper arm strength (grip strength). Data has been presented by dominant and non-dominant hand. Analysis was done using an RCM, which included visit in years (as a continuous variable), and baseline efficacy as fixed effects, the intercept and the linear slope of visit as

random effect, and individual participants as participant effect. ITT population included all participants who enrolled in the study.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Pamrevlumab			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: newton				
least squares mean (standard error)				
Dominant Grip Best Result	-2.52 (± 3.610)			
Non-Dominant Grip Best Result	-1.31 (± 3.591)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Upper Arm (Biceps Brachii MRI) Muscle Fat and Fibrosis Score, as Measured by MRI at Week 104

End point title	Change From Baseline in Upper Arm (Biceps Brachii MRI) Muscle Fat and Fibrosis Score, as Measured by MRI at Week 104

End point description:

T2-mapping with MRI was conducted to measure upper arm muscle fibrosis and fat in the biceps brachii muscle. Analysis was done using an RCM, which included visit in years (as a continuous variable), and baseline efficacy as fixed effects, the intercept and the linear slope of visit as random effect, and individual participants as participant effect. The visual score for muscle fat and fibrosis will be assessed using a modified 5-point Mercuri score in which 0 = normal muscle appearance and 5 = complete replacement of muscle by connective tissue and fat, where a lower score indicated visually healthier muscle. Change from baseline was calculated as the score at Week 104 – the score at baseline. ITT population included all participants who enrolled in the study. Here, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Pamrevlumab			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: unit on scale				
least squares mean (standard error)	-2.22 (± 1.088)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Cardiac Fibrosis (Scar Mass), as Measured by Magnetic Resonance Imaging (MRI) at Week 104

End point title	Change From Baseline in Cardiac Fibrosis (Scar Mass), as Measured by Magnetic Resonance Imaging (MRI) at Week 104

End point description:

Cardiac MRI was used to assess the cardiac fibrosis by detecting the presence of late gadolinium enhancement (LGE), a marker for myocardial fibrosis. Analysis was done using an RCM, which included visit in years (as a continuous variable), and baseline efficacy as fixed effects, the intercept and the linear slope of visit as random effect, and individual participants as participant effect. ITT population included all participants who enrolled in the study. Here, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Pamrevlumab			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: grams				
least squares mean (standard error)	3.74 (± 4.475)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fat Fraction Percentage (%F), as Measured by MRI at Week 104

End point title	Change From Baseline in Fat Fraction Percentage (%F), as Measured by MRI at Week 104

End point description:

Analysis was done using an RCM, which included visit in years (as a continuous variable), and baseline efficacy as fixed effects, the intercept and the linear slope of visit as random effect, and individual participants as participant effect. ITT population included all participants who enrolled in the study. Here, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Pamrevlumab			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percentage of fat				
least squares mean (standard error)	4.49 (± 2.030)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to Week 104	
Adverse event reporting additional description:	
Safety population included participants who received at least one dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	Pamrevlumab
Reporting group description:	
Participants received pamrevlumab 35 mg/kg by IV infusion every 2 weeks for a minimum of 104 weeks.	

Serious adverse events	Pamrevlumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 21 (28.57%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skull fracture			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			

subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Food poisoning			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Metabolic acidosis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Pamrevlumab		
Total subjects affected by non-serious adverse events subjects affected / exposed	21 / 21 (100.00%)		
Vascular disorders Flushing subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 2		
Hypertension subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Surgical and medical procedures Tooth extraction subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
General disorders and administration site conditions Chest pain subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Chills subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Axillary pain subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Pyrexia subjects affected / exposed occurrences (all)	8 / 21 (38.10%) 17		
Cyst subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Extravasation subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Fatigue subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		

Infusion site pain subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Injection site pain subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Malaise subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 2		
Nodule subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Pain subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Peripheral swelling subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 2		
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 3		
Respiratory, thoracic and mediastinal disorders Paranasal sinus discomfort subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Dyspnoea subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Productive cough subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Nasal congestion			

subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	5		
Rhinorrhoea			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	8		
Oropharyngeal pain			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	10		
Sinus congestion			
subjects affected / exposed	6 / 21 (28.57%)		
occurrences (all)	12		
Cough			
subjects affected / exposed	9 / 21 (42.86%)		
occurrences (all)	20		
Throat irritation			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Sleep apnoea syndrome			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Depression			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Affect lability			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	4		
Investigations			
Cystatin C increased			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Weight decreased			

subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Blood pressure increased			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Bone density decreased			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Electrocardiogram PR shortened			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Eosinophil count increased			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Neutrophil count increased			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
White blood cell count increased			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Ankle fracture			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Bone contusion			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Compression fracture			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Contusion			

subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Foot fracture			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Procedural nausea			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Scratch			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Soft tissue injury			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Spinal compression fracture			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Sunburn			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Wound			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Supraventricular extrasystoles			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		

Myocardial fibrosis subjects affected / exposed occurrences (all) Palpitations subjects affected / exposed occurrences (all)	 1 / 21 (4.76%) 1 3 / 21 (14.29%) 3		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Migraine subjects affected / exposed occurrences (all) Sinus headache subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all)	 14 / 21 (66.67%) 66 3 / 21 (14.29%) 4 2 / 21 (9.52%) 3 2 / 21 (9.52%) 2 1 / 21 (4.76%) 1 1 / 21 (4.76%) 1		
Blood and lymphatic system disorders Lymphocytosis subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	 1 / 21 (4.76%) 1 1 / 21 (4.76%) 1 1 / 21 (4.76%) 1		
Ear and labyrinth disorders			

Ear swelling			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Ear pain			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Cerumen impaction			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Eye disorders			
Cataract			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	10 / 21 (47.62%)		
occurrences (all)	13		
Tooth impacted			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	3		
Constipation			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Aphthous ulcer			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Abdominal discomfort			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	4		
Dyspepsia			

subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 4		
Abdominal distension subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Diarrhoea subjects affected / exposed occurrences (all)	5 / 21 (23.81%) 6		
Nausea subjects affected / exposed occurrences (all)	7 / 21 (33.33%) 11		
Abdominal pain upper subjects affected / exposed occurrences (all)	5 / 21 (23.81%) 8		
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Skin discolouration subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Rash subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Erythema subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Dry skin subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Renal and urinary disorders			
Nephrolithiasis subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 2		
Endocrine disorders			

Adrenal insufficiency			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	8 / 21 (38.10%)		
occurrences (all)	13		
Myalgia			
subjects affected / exposed	5 / 21 (23.81%)		
occurrences (all)	6		
Arthralgia			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	4		
Joint swelling			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Limb discomfort			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Musculoskeletal disorder			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Osteoporosis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 21 (52.38%)		
occurrences (all)	27		
Upper respiratory tract infection			
subjects affected / exposed	5 / 21 (23.81%)		
occurrences (all)	6		
Sinusitis			

subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	6		
Influenza			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Pneumonia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Candida infection			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Cellulitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Eye infection			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Hordeolum			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Localised infection			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 August 2015	It included following changes: - Deleted exploratory endpoint: Effect of concomitant corticosteroid treatment on LVEF and cardiac fibrosis. - Inclusion criteria was updated to specify wheelchair dependent for <5 years. - Inclusion criteria was updated to increased length of stable regimen of heart failure cardiac medications prior to screening from 6 weeks to 3 months. - Exclusion criteria was updated to mention the need for intravenous diuretics or inotropic support increased from within 6 weeks to at least 3 months prior to screening; and hospitalization for a heart failure exacerbation or arrhythmia increased from last 6 weeks to last 3 months. - Deleted inclusion criteria for the option of no corticosteroid use for at least 6 months prior to screening and throughout the study participation. - Mandated stable treatment with corticosteroids at baseline. - Changed duration of follow-up period from 6 weeks to 10 weeks. - Allowed use of deflazacort, if regarded by the principal investigator as standard of care.
06 May 2016	It included following changes: - Replaced forearm muscle MRI with upper arm (bicep) muscle MRI. - Revised Inclusion criterion 8 to allow only enrollment of participants with a ppFVC ≥50. - Dosing based on body weight measured at screening and every 3 months thereafter. - Safety follow-up period reduced from 10 weeks to 4 weeks after the last dose of study drug. - Infusion rate of FG-3019 not to exceed 150 cubic centimeters (cc)/hour. Adjustments to lower infusion rate allowed per investigator's clinical judgment. - Clarified requirement for local safety labs (including hematocrit) to be drawn prior to conduct of MRIs. - Added stipulation that home health care may be considered for administration of future pamrevlumab infusions during the conduct of the study.
09 December 2016	It included following changes: - Replacement of FG-3019 with pamrevlumab. - Decreased study duration from 104 weeks to 52 weeks with option to continue an additional 26 weeks (78 weeks total) for participants who achieve a ≤5% decline from baseline in ppFVC by Week 52. - Updated time on study to reflect weeks vs years (ie, change from 1 year to 52 weeks). - Removed Interim Analysis at Week 52. - Deleted Inclusion criterion: Wheelchair dependency <5 years. - Revised Inclusion criterion to only allow enrollment of participants with a ppFVC between 40 and 90, inclusive. Deleted "estimated annual decline of FVC (% predicted) of ≥5% based upon at least 2 PFTs done in the previous 18 months, in addition to the screening FVC" from Inclusion criterion. Changed criteria to "At least one historical FVC % predicted value within 18 months of baseline". - Modified Inclusion criterion to "Participants currently receiving heart failure cardiac medications (for example, angiotensin converting enzyme inhibitors, angiotensin-receptor blockers, and beta-blockers) must achieve a stable regimen for at least 3 months prior to screening". - Modified Exclusion criterion to update time frame of anticipated spine surgery from 2 years to 78 weeks. - Modified Exclusion criterion to clarify that the use of another investigational drug or another approved product for DMD (for example, eteplirsen) within 28 days or 5 half-lives of the product, whichever was longer, prior to first Screening Visit, with the exception of deflazacort, was exclusionary. Allowed use of deflazacort if regarded by the principal investigator as standard of care. - Clarified that any approved product for DMD (for example, eteplirsen) during study treatment was prohibited.

10 July 2017	It included following changes: -Sample size changed to reflect that study may enroll up to 32 participants dependent on outcome of interim analysis. - Extended treatment duration from 52 weeks plus extension to 104 weeks; removed extension and added interim analysis. - Changed primary endpoint to annual change in ppFVC during treatment. - Changed Exclusion criteria to reflect increased treatment duration. - Amended language to reflect that only the first infusion was based on the screening weight. - Updated to reflect that infusion reactions are considered an identified risk of pamrevlumab administration and deleted that they did not recur with readministration.
14 November 2017	It included following changes: - Primary efficacy endpoint changed from "annual change in ppFVC during treatment with pamrevlumab" to "annual change from baseline to Week 104 in ppFVC during treatment with pamrevlumab". - Removed sentence about analysis method ("t-test") for primary efficacy endpoint. - Modified number of participants required for interim analysis from "at least 12" to "at least 10 to 12". - Clarified PK sample time-point collection. - Extended treatment duration from 104 weeks to 156 weeks with exploratory analyses at Week 156.
27 September 2019	It included following changes: - Addition of Appendix: OLE for all participants who completed 104 weeks of treatment on the main study and completed end of treatment (EOT). Modifications made in main study to address addition of Appendix. - Added Respiratory Muscles and Diaphragm MRI in OLE.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported