Clinical trial results:
A Multicenter, Open-Label Extension Study to Evaluate the Long Term Safety of PF-06252616 in Boys With Duchenne Muscular Dystrophy

Summary

EudraCT number	2016-001615-21
Trial protocol	GB IT BG
Global end of trial date	22 November 2018

Results information

Result version number	v1 (current)
This version publication date	29 May 2019
First version publication date	29 May 2019

Trial information

Trial identification

Sponsor protocol code	B5161004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02907619
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer Clinical Trials.gov Call Center, Pfizer, Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001763-PIP01-15
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final

Date of interim/final analysis	06 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 November 2018
Global end of trial reached?	Yes
Global end of trial date	22 November 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to assess the long term safety, efficacy, pharmacokinetics (PK), immunogenicity and pharmacodynamics (PD) of intravenous (IV) dosing of PF-06252616 (domagrozumab) in boys with Duchenne muscular dystrophy (DMD).

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy:

Study B5161004 was an open-label extension (OLE) to study B5161002.
The parent study B5161002 was a Phase 2, randomized, 2-period, blinded, placebo controlled study to evaluate the safety, efficacy, PK and PD of domagrozumab administered to ambulatory boys diagnosed with DMD. A total of 120 male subjects with ages of 6 to <16 years were randomized to 1 of 3 sequence groups so that the subjects received investigational product and/or placebo for approximately 96 weeks (2 treatment periods of approximately 48 weeks each).

Evidence for comparator: -

Actual start date of recruitment	13 October 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 Kingdom: 6
Country: Number of subjects enrolled	United States: 39
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Japan: 4
Worldwide total number of subjects	59
EEA total number of subjects	8

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)	59
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 61 subjects screened, 1 subject failed at screening due to not meeting entrance criteria and 1 was not assigned due to study termination by the sponsor. The remaining 59 subjects were assigned to the study treatment and were treated with domagrozumab.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence 1

Arm description:

In study B5161002 (parent study) subjects randomized to Sequence group 1 received domagrozumab (PF-06252616) in a dose escalating fashion (5, 20 and 40 mg/kg), starting with the lowest dose in Period 1. At each dose level, dosing was administered over 2 hours by intravenous (IV) infusion every 4 weeks for a total of 16 weeks. In Period 2, subjects received domagrozumab (PF-06252616) at the maximum tolerated dose in Period 1 every 4 weeks for a total of 48 weeks. There was no pause between Period 1 and Period 2 (48 weeks each). In study B5161004 (OLE) subjects received domagrozumab 40 mg/kg (the maximum tolerated dose from B5161002) every 4 weeks. The OLE study reports subjects within the treatment assignment they received in the parent study.

Arm type	Experimental
Investigational medicinal product name	PF-06252616
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

PF-06252616 (domagrozumab) 40 mg/kg was infused over 2 hours (-15 or +30 minutes) which included the flush time in this OLE study.

Arm title	Sequence 2

Arm description:

In study B5161002 (parent study) subjects randomized to Sequence group 2 received domagrozumab (PF-06252616) in a dose escalating fashion (5, 20 and 40 mg/kg), starting with the lowest dose in Period 1. At each dose level, dosing was administered over 2 hours by IV infusion every 4 weeks for a total of 16 weeks. In Period 2, subjects received placebo. There was no pause between Period 1 and Period 2 (48 weeks each). In study B5161004 (OLE) subjects received domagrozumab 40 mg/kg (the maximum tolerated dose from B5161002) every 4 weeks. The OLE study reports subjects within the treatment assignment they received in the parent study.

Arm type	Experimental
Investigational medicinal product name	PF-06252616
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Routes of administration	Intravenous use

Dosage and administration details:

PF-06252616 (domagrozumab) 40 mg/kg was infused over 2 hours (-15 or +30 minutes) which included the flush time in this OLE study.

Arm title	Sequence 3

Arm description:

In study B5161002 (parent study) subjects randomized to Sequence group 3 received placebo in Period 1 (48 weeks). In Period 2, subjects received domagrozumab (PF-06252616) in a dose escalating fashion (5, 20 and 40 mg/kg), starting with the lowest dose. At each dose level, dosing was administered over 2 hours by IV infusion every 4 weeks for a total of 16 weeks. There was no pause between Period 1 and Period 2 (48 weeks each). In study B5161004 (OLE) subjects received domagrozumab 40 mg/kg (the maximum tolerated dose from B5161002) every 4 weeks. The OLE study reports subjects within the treatment assignment they received in the parent study.

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Investigational medicinal product name	PF-06252616
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Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

PF-06252616 (domagrozumab) 40 mg/kg was infused over 2 hours (-15 or +30 minutes) which included the flush time in this OLE study.

Number of subjects in period 1	Sequence 1	Sequence 2	Sequence 3
Started	19	20	20
Completed	0	0	0
Not completed	19	20	20
Study Terminated by Sponsor	18	18	19
Other	-	1	-
Adverse event, serious fatal	-	-	1
No Longer Willing To Participate In Study	1	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Sequence 1
Reporting group description:	
In study B5161002 (parent study) subjects randomized to Sequence group 1 received domagrozumab (PF-06252616) in a dose escalating fashion (5, 20 and 40 mg/kg), starting with the lowest dose in Period 1. At each dose level, dosing was administered over 2 hours by intravenous (IV) infusion every 4 weeks for a total of 16 weeks. In Period 2, subjects received domagrozumab (PF-06252616) at the maximum tolerated dose in Period 1 every 4 weeks for a total of 48 weeks. There was no pause between Period 1 and Period 2 (48 weeks each). In study B5161004 (OLE) subjects received domagrozumab 40 mg/kg (the maximum tolerated dose from B5161002) every 4 weeks. The OLE study reports subjects within the treatment assignment they received in the parent study.	
Reporting group title	Sequence 2
Reporting group description:	
In study B5161002 (parent study) subjects randomized to Sequence group 2 received domagrozumab (PF-06252616) in a dose escalating fashion (5, 20 and 40 mg/kg), starting with the lowest dose in Period 1. At each dose level, dosing was administered over 2 hours by IV infusion every 4 weeks for a total of 16 weeks. In Period 2, subjects received placebo. There was no pause between Period 1 and Period 2 (48 weeks each). In study B5161004 (OLE) subjects received domagrozumab 40 mg/kg (the maximum tolerated dose from B5161002) every 4 weeks. The OLE study reports subjects within the treatment assignment they received in the parent study.	
Reporting group title	Sequence 3
Reporting group description:	
In study B5161002 (parent study) subjects randomized to Sequence group 3 received placebo in Period 1 (48 weeks). In Period 2, subjects received domagrozumab (PF-06252616) in a dose escalating fashion (5, 20 and 40 mg/kg), starting with the lowest dose. At each dose level, dosing was administered over 2 hours by IV infusion every 4 weeks for a total of 16 weeks. There was no pause between Period 1 and Period 2 (48 weeks each). In study B5161004 (OLE) subjects received domagrozumab 40 mg/kg (the maximum tolerated dose from B5161002) every 4 weeks. The OLE study reports subjects within the treatment assignment they received in the parent study.	

Reporting group values	Sequence 1	Sequence 2	Sequence 3
Number of subjects	19	20	20
Age categorical Units: Subjects			
7 - < 8 years	1	0	0
8 - < 9 years	4	2	2
9 - < 10 years	8	1	3
10 - < 11 years	4	9	1
11 - < 12 years	2	8	14
Age Continuous Units: years			
arithmetic mean	9.1	10.2	10.4
standard deviation	± 1.0	± 0.9	± 1.1
Sex: Female, Male Units: Subjects			
MALE	19	20	20
Race Units: Subjects			
White	18	17	18
Asian	1	2	2
Other	0	1	0

Weight			
Units: Kilograms			
arithmetic mean	32.9	36.8	41.5
standard deviation	± 8.9	± 12.3	± 15.9
Height			
Units: Centimeters			
arithmetic mean	127.6	131.5	132.8
standard deviation	± 7.4	± 12.5	± 9.4

Reporting group values	Total		
Number of subjects	59		
Age categorical			
Units: Subjects			
7 - < 8 years	1		
8 - < 9 years	8		
9 - < 10 years	12		
10 - < 11 years	14		
11 - < 12 years	24		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Subjects			
MALE	59		
Race			
Units: Subjects			
White	53		
Asian	5		
Other	1		
Weight			
Units: Kilograms			
arithmetic mean			
standard deviation	-		
Height			
Units: Centimeters			
arithmetic mean			
standard deviation	-		

Subject analysis sets

Subject analysis set title	Total
Subject analysis set type	Intention-to-treat

Subject analysis set description:
This is the sum of all subjects in the study

Reporting group values	Total		
Number of subjects	59		
Age categorical			
Units: Subjects			
7 - < 8 years	1		

8 - < 9 years	8		
9 - < 10 years	12		
10 - < 11 years	14		
11 - < 12 years	24		
Age Continuous			
Units: years			
arithmetic mean	9.9		
standard deviation	± 1.1		
Sex: Female, Male			
Units: Subjects			
MALE	59		
Race			
Units: Subjects			
White	53		
Asian	5		
Other	1		
Weight			
Units: Kilograms			
arithmetic mean	37.2		
standard deviation	± 13.1		
Height			
Units: Centimeters			
arithmetic mean	130.7		
standard deviation	± 10.0		

End points

End points reporting groups

Reporting group title	Sequence 1

Reporting group description:

In study B5161002 (parent study) subjects randomized to Sequence group 1 received domagrozumab (PF-06252616) in a dose escalating fashion (5, 20 and 40 mg/kg), starting with the lowest dose in Period 1. At each dose level, dosing was administered over 2 hours by intravenous (IV) infusion every 4 weeks for a total of 16 weeks. In Period 2, subjects received domagrozumab (PF-06252616) at the maximum tolerated dose in Period 1 every 4 weeks for a total of 48 weeks. There was no pause between Period 1 and Period 2 (48 weeks each). In study B5161004 (OLE) subjects received domagrozumab 40 mg/kg (the maximum tolerated dose from B5161002) every 4 weeks. The OLE study reports subjects within the treatment assignment they received in the parent study.

Reporting group title	Sequence 2

Reporting group description:

In study B5161002 (parent study) subjects randomized to Sequence group 2 received domagrozumab (PF-06252616) in a dose escalating fashion (5, 20 and 40 mg/kg), starting with the lowest dose in Period 1. At each dose level, dosing was administered over 2 hours by IV infusion every 4 weeks for a total of 16 weeks. In Period 2, subjects received placebo. There was no pause between Period 1 and Period 2 (48 weeks each). In study B5161004 (OLE) subjects received domagrozumab 40 mg/kg (the maximum tolerated dose from B5161002) every 4 weeks. The OLE study reports subjects within the treatment assignment they received in the parent study.

Reporting group title	Sequence 3

Reporting group description:

In study B5161002 (parent study) subjects randomized to Sequence group 3 received placebo in Period 1 (48 weeks). In Period 2, subjects received domagrozumab (PF-06252616) in a dose escalating fashion (5, 20 and 40 mg/kg), starting with the lowest dose. At each dose level, dosing was administered over 2 hours by IV infusion every 4 weeks for a total of 16 weeks. There was no pause between Period 1 and Period 2 (48 weeks each). In study B5161004 (OLE) subjects received domagrozumab 40 mg/kg (the maximum tolerated dose from B5161002) every 4 weeks. The OLE study reports subjects within the treatment assignment they received in the parent study.

Subject analysis set title	Total
Subject analysis set type	Intention-to-treat

Subject analysis set description:

This is the sum of all subjects in the study

Primary: Number of Subjects With Dose Reduced or Temporary Discontinuation Due to AEs

End point title	Number of Subjects With Dose Reduced or Temporary Discontinuation Due to AEs[1]

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation subject administered a product; the event does not need to have a causal relationship with the treatment or usage. Treatment-related AEs were determined by the investigator. The number of subjects with dose reduced or temporary discontinuation due to both all-causality and treatment-related TEAEs are presented below. The Safety Analysis Set was defined as all subjects who had received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

2 Years

Notes:

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

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
Due to All-causality AEs	0	0	0	0
Due to Treatment-related AEs	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjcts With Severe Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Subjcts With Severe Treatment-Emergent Adverse Events (TEAEs)[2]

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation subject administered a product; the event does not need to have a causal relationship with the treatment or usage. A serious adverse event (SAE) was any untoward medical occurrence at any dose that resulted in death; was life threatening; required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity; resulted in congenital anomaly/birth defect. AEs included both SAEs and AEs. TEAEs were AEs occurred following the start of treatment or AEs increasing in severity during treatment.Severe TEAEs were TEAEs that interfered significantly with subjects' usual function.Treatment-related TEAEs were determined by the investigator. The number of subjects with severe all-causalities and treatment-related TEAEs are presented below. The Safety Analysis Set was defined as all subjects who had received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

2 Years

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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
All Causalities	3	0	1	4
Treatment-related	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Discontinued From the Study Due to TEAEs

End point title	Number of Subjects Discontinued From the Study Due to

End point description:

An AE was any untoward medical occurrence in a clinical investigation subject administered a product;

the event does not need to have a causal relationship with the treatment or usage. TEAEs were AEs occurred following the start of treatment or AEs increasing in severity during treatment. Treatment-related TEAEs were determined by the investigator. The number of subjects discontinued from the study due to both all-causality and treatment-related TEAEs are presented below. The Safety Analysis Set was defined as all subjects who had received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

2 Years

Notes:

[3] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
Due to All-causality AEs	0	0	1	1
Due to Treatment-related AEs	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Hematology

End point title	Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Hematology[4]

End point description:

Hematology evaluation included: hemoglobin, hematocrit, red blood cell (RBC) count, platelets, RBC morphology, white blood cell (WBC) count, absolute lymphocytes, absolute atypical lymphocytes, absolute total neutrophils, absolute total neutrophils count, absolute band cells, absolute basophils, absolute eosinophils and absolute monocytes.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. (ULN=Upper Limit of Normal; LLN=Lower Limit of Normal).

End point type	Primary

End point timeframe:

2 Years

Notes:

[4] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[5]	20[6]	20[7]	59[8]
Units: Subjects				
Hemoglobin <0.8 × LLN	0	0	0	0
Hematocrit <0.8 × LLN	0	0	0	0
Red Blood Cell (RBC) count <0.8 × LLN	0	0	0	0
Platelets <0.5 × LLN	0	0	0	0

Platelets >1.75 × ULN	0	0	0	0
RBC Morphology >0	0	1	0	1
White Blood Cell (WBC) count <0.6 × LLN	0	0	0	0
WBC count >1.5 × ULN	0	0	0	0
Absolute Lymphocytes <0.8 × LLN	0	0	0	0
Absolute lymphocytes >1.2 × ULN	0	0	0	0
Absolute atypical lymphocytes >0	1	99999	99999	1
Absolute total neutrophils <0.8 × LLN	0	0	0	0
Absolute total neutrophils >1.2 × ULN	3	1	2	6
Absolute total neutrophil count <1.35 × 10^3/mcL	0	0	0	0
Absolute total neutrophil count >8.15 × 10^3/mcL	6	1	5	12
Absolute band cells >0.27 × 10^3/mcL	0	99999	99999	0
Absolute basophils >1.2 × ULN	0	0	0	0
Absolute eosinophils >1.2 × ULN	1	0	1	2
Absolute monocytes >1.2 × ULN	1	0	1	2

Notes:

[5] - One subject analyzed for absolute atypical lymphocytes and absolute band cells

[6] - If no evaluable data collected, 99999 was entered instead.

[7] - If no evaluable data collected, 99999 was entered instead.

[8] - One subject analyzed for absolute atypical lymphocytes and absolute band cells

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjecs With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Coagulation

End point title	Number of Subjecs With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Coagulation[9]

End point description:

Coagulation evaluation included activated partial thromboplastin time (aPTT) and prothrombin time (PT). (ULN=Upper Limit of Normal).
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication.
Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004.

End point type	Primary

End point timeframe:

2 Years

Notes:

[9] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
APTT >1.1 x ULN	0	0	1	1
Prothrombin (PT) >1.1 x ULN	1	0	1	2

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Liver Function

End point title	Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Liver Function[10]

End point description:

Liver function evaluation included: total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), alkaline phosphatase, total protein, albumin and glutamate dehydrogenase.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. (LLN=Lower Limit of Normal; ULN=Upper Limit of Normal).

End point type	Primary

End point timeframe:

2 Years

Notes:

[10] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
Total Bilirubin >1.5 x ULN	0	0	0	0
Aspartate Aminotransferase (AST) >3.0 x ULN	16	16	15	47
Alanine Aminotransferase (ALT) >3.0 x ULN	19	18	19	56
GGT >3.0 x ULN	0	0	0	0
Alkaline Phosphatase >3.0 x ULN	0	0	0	0
Total Protein <0.8 x LLN	0	0	0	0
Total Protein >1.2 x ULN	0	0	0	0
Albumin <0.8 x LLN	0	0	0	0
Albumin >1.2 x ULN	0	0	0	0
Glutamate Dehydrogenase >1.0 x ULN	0	0	1	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Renal Function

End point title	Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Renal Function[11]

End point description:

Renal function evaluation included: blood urea nitrogen (BUN), creatinine and uric acid.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication.
Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. (ULN=Upper Limit of Normal).

End point type	Primary

End point timeframe:

2 Years

Notes:

[11] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
Blood Urea Nitrogen (BUN) >1.3 x ULN	0	0	0	0
Creatinine >1.3 x ULN	0	0	0	0
Uric Acid >1.2 x ULN	1	0	0	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Electrolytes

End point title	Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Electrolytes[12]

End point description:

Electrolytes evaluation included: sodium, potassium, chloride, calcium, phosphate and bicarbonate.
Number of subjects with iron abnormalities was reported in different age groups.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. (LLN=Lower Limit of Normal, ULN=Upper Limit of Normal).

End point type	Primary

End point timeframe:

2 Years

Notes:

[12] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
Sodium <0.95 x LLN	0	0	0	0
Sodium >1.05 x ULN	0	0	0	0
Potassium <0.9 x LLN	0	0	0	0
Potassium >1.1 x ULN	1	0	0	1
Chloride <0.9 x LLN	0	0	0	0
Chloride >1.1 x ULN	0	0	0	0
Calcium <0.9 x LLN	0	0	0	0
Calcium >1.1 x ULN	0	0	0	0
Phosphate <0.8 x LLN	0	0	0	0
Phosphate >1.2 x ULN	0	0	0	0
Bicarbonate (venous) <0.9 x LLN	0	0	0	0
Bicarbonate (venous) >1.1 x ULN	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Hormones

End point title	Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Hormones[13]

End point description:

Hormone evaluations included free thyroxine (T4), thyroid stimulating hormone (TSH), lutenizing hormone (LH), follicle stimulating hormone (FSH), and androstenedione. Numbers of subjects with abnormalities of LH, FSH and androstenedione were reported in different age groups.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. N=x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. (LLN=Lower Limit of Normal, ULN=Upper Limit of Normal).

End point type	Primary

End point timeframe:

2 Years

Notes:

[13] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	18	18[14]	17[15]	53
Units: Subjects				
T4 (free) <0.8 x LLN (N=18,18,17,53)	0	0	0	0
T4 (free) >1.2 x ULN (N=18,18,17,53)	0	0	0	0
TSH <0.8 x LLN (N=18,18,17,53)	0	1	0	1
TSH >1.2 x ULN (N=18,18,17,53)	0	0	0	0
LH (7years - <9 years) <0.3mIU/mL (N=2,0,0,2)	0	99999	99999	0

LH(7years -<9 years) >2.8mIU/mL (N=2,0,0,2)	0	99999	99999	0
LH (9years-<11 years) <0.3mIU/mL (N=13,5,4,22)	8	5	3	16
LH (9years-<11 years) >2.8mIU/mL (N=13,5,4,22)	0	0	0	0
LH (11years-<12 years) <0.3mIU/mL (N=3,6,2,11)	2	3	2	7
LH (11years-<12 years) >1.8mIU/mL (N=3,6,2,11)	0	0	0	0
LH(12years-<13 years) <0.3 mIU/mL (N=1,8,11,20)	0	5	8	13
LH(12years-<13 years) >4.0mIU/mL (N=1,8,11,20)	0	0	0	0
LH(13years-<14 years) <0.3mIU/mL (N=1,1,1,3)	1	0	1	2
LH(13years-<14 years) >6.0mIU/mL (N=1,1,1,3)	0	0	0	0
FSH(7years-<9 years) >4.10mIU/mL (N=2,0,0,2)	0	99999	99999	0
FSH (9years-<11 years) >4.50mIU/mL (N=13,5,4,22)	0	0	0	0
FSH (11years-<12 years) <0.40mIU/mL (N=3,6,2,11)	0	0	0	0
FSH (11years-<12 years) >8.90mIU/mL (N=3,6,2,11)	0	0	0	0
FSH (12years-<13 years) <0.50mIU/mL (N=1,8,11,20)	0	0	0	0
FSH (12years-<13 years) >10.50mIU/mL (N=1,8,11,20)	0	0	0	0
FSH (13years-<14 years) <0.70mIU/mL (N=1,1,1,3)	1	0	1	2
FSH (13years-<14 years) >10.80mIU/mL (N=1,1,1,3)	0	0	0	0
Androstenedione(7-<10years) <3ng/dL(N=6,2,4,12)	0	0	2	2
Androstenedione(7-<10 years) >31ng/dL(N=6,2,4,12)	1	1	0	2
Androstenedione(10-<12years) <7ng/dL(N=12,9,2,23)	5	3	1	9
Androstenedione(10-<12years) >41ng/dL(N=12,9,2,23)	1	0	0	1
Androstenedione(12-<14years) <11ng/dL(N=1,8,11,20)	1	4	6	11
Androstenedione(12-<14years) >64ng/dL(N=1,8,11,20)	0	0	0	0

Notes:

[14] - If no evaluable data collected, 99999 was entered instead.

[15] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Clinical Chemistry

End point title	Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Clinical Chemistry[16]

End point description:

Clinical chemistry evaluation included glucose, creatine kinase (CK), troponin I, amylase, iron binding capacity, unsaturated iron binding capacity, transferrin saturation, iron and ferritin.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. N represents the corresponding number of evaluable subjects in each arm where not all subjects were analyzed. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.
Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. (LLN=Lower Limit of Normal, ULN=Upper Limit of Normal).

End point type	Primary

End point timeframe:

2 Years

Notes:

[16] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
Glucose <0.6 x LLN	0	0	0	0
Glucose >1.5 x ULN	0	0	0	0
CK >2.0 x ULN	19	20	20	59
Troponin I >3.0 x ULN (N = 19, 18, 17, 54)	4	4	1	9
Amylase > 1.5 x ULN	0	0	1	1
Iron Binding Capacity <37.6 mcg/dL	0	0	0	0
Unsaturated Iron Binding Capacity <130 mcg/dL	3	4	3	10
Unsaturated Iron Binding Capacity >375 mcg/dL	0	0	0	0
Transferrin Saturation < 20%	0	3	2	5
Transferrin Saturation > 50%	7	4	6	17
Iron 1Y<=Age<11Y <50 (N = 17, 8, 6, 31)	0	0	1	1
Iron 1Y<=Age<11Y >120 (N = 17, 8, 6, 31)	12	2	2	16
Iron 11Y<=Age<18Y <50 (N = 4, 15, 15, 34)	0	3	0	3
Iron 11Y<=Age<18Y >170 (N = 4, 15, 15, 34)	0	1	1	2
Ferritin <15 ng/mL	4	6	5	15
Ferritin >140 ng/mL	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Urinalysis

End point title	Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Urinalysis[17]

End point description:

Urinalysis Microscopy included: urine red blood cell (RBC), urine white blood cell (WBC), urine uric acid crystals, urine calcium oxalate crystals, urine amorphous crystals, urine bacteria, urine microscopic exam.
Urinalysis Dipstick included: urine pH, urine glucose, urine ketones, urine protein, urine blood/hemoglobin, urine nitrite, urine leukocyte esterase.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. Not all subjects had evaluable data at each category. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004.

End point type	Primary

End point timeframe:

2 Years

Notes:

[17] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20[18]	20[19]	59
Units: Subjects				
Microscopy - Urine RBC >=20	0	0	0	0
Microscopy - Urine WBC >=20	0	0	0	0
Microscopy-Urine Uric Acid Crystals - Present	1	99999	99999	1
Microscopy-Urine Calcium Oxalate Crystals -Present	4	7	4	15
Microscopy-Urine Amorphous Crystals - Present	3	3	2	8
Microscopy - Urine Bacteria >20	0	0	99999	0
Microscopy-Urine Microscopic Exam - Positive	8	11	7	26
Dipstick - Urine pH <4.5	0	0	0	0
Dipstick - Urine pH >8	0	1	0	1
Dipstick - urine glucose >=1	0	0	0	0
Dipstick - urine ketones >=1	0	1	1	2
Dipstick - urine protein >=1	0	0	0	0
Dipstick - urine blood/hemoglobin >=1	0	0	0	0
Dipstick - Urine nitrite >=1	0	0	0	0
Dipstick - Urine Leukocyte Esterase >=1	0	1	0	1

Notes:

[18] - If no evaluable data collected, 99999 was entered instead.

[19] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Fecal Blood

End point title	Number of Subjects With Laboratory Test Abnormalities (Without Regard to B5161004 Baseline Abnormality) - Fecal Blood[20]

End point description:

Number of subjects with fecal occult blood detected is presented. Number of subjects with blood detected in fecal samples is presented.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in

Sequence groups 1, 2, 3 and Total. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. (ULN=Upper Limit of Normal).

End point type	Primary

End point timeframe:

2 Years

Notes:

[20] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
Fecal Blood - Positive (N = 19, 17, 17, 53)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Data of Serum Ferritin, Serum Iron and % Transferrin Saturation Meeting Categorical Summarization Criteria - B5161004 Baseline

End point title	Number of Subjects With Data of Serum Ferritin, Serum Iron and % Transferrin Saturation Meeting Categorical Summarization Criteria - B5161004 Baseline[21]

End point description:

Subjects were asked to fast for at least 8 hours prior to collection of blood to evaluate serum iron, serum ferritin and % transferrin saturation. The unit of iron was mcg/dL; the unit of ferritin was ng/mL; the unit of %transferrin saturation was %.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Baseline, Weeks 13, 25, 37, 49, 61, 73 and 85. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

Notes:

[21] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[22]	20[23]	20[24]	59[25]
Units: Subjects				
Iron-Baseline <120	13	18	10	41
Iron-Baseline 120 - <144	3	2	6	11
Iron-Baseline 144 - <200	3	0	4	7
Iron-Baseline >=200	0	0	0	0
Iron-Week 13 <120	10	15	9	34
Iron-Week 13 120 - <144	3	0	7	10

Iron-Week 13 144 - <200	2	1	1	4
Iron-Week 13 >=200	0	0	0	0
Iron-Week 25 <120	8	10	8	26
Iron-Week 25 120 - <144	3	0	4	7
Iron-Week 25 144 - <200	1	2	1	4
Iron-Week 25 >=200	0	0	0	0
Iron-Week 37 <120	5	6	10	21
Iron-Week 37 120 - <144	1	3	2	6
Iron-Week 37 144 - <200	2	0	0	2
Iron-Week 37 >=200	0	0	0	0
Iron-Week 49 <120	6	3	6	15
Iron-Week 49 120 - <144	1	0	1	2
Iron-Week 49 144 - <200	0	3	1	4
Iron-Week 49 >=200	0	0	0	0
Iron-Week 61 <120	1	2	2	5
Iron-Week 61 120 - <144	1	1	1	3
Iron-Week 61 144 - <200	1	1	0	2
Iron-Week 61 >=200	0	0	0	0
Iron-Week 73 <120	1	1	2	4
Iron-Week 73 120 - <144	1	0	0	1
Iron-Week 73 144 - <200	0	1	0	1
Iron-Week 73 >=200	0	0	0	0
Iron-Week 85 <120	0	1	1	2
Iron-Week 85 120 - <144	0	0	0	0
Iron-Week 85 144 - <200	0	0	0	0
Iron-Week 85 >=200	0	0	0	0
Ferritin-Baseline <140	19	20	20	59
Ferritin-Baseline >=140	0	0	0	0
Ferritin-Week 13 <140	14	17	16	47
Ferritin-Week 13 >=140	0	0	0	0
Ferritin-Week 25 <140	12	12	13	37
Ferritin-Week 25 >=140	0	0	0	0
Ferritin-Week 37 <140	7	9	12	28
Ferritin-Week 37 >=140	0	0	0	0
Ferritin-Week 49 <140	7	6	8	21
Ferritin-Week 49 >=140	0	0	0	0
Ferritin-Week 61 <140	2	4	3	9
Ferritin-Week 61 >=140	0	0	0	0
Ferritin-Week 73 <140	2	2	2	6
Ferritin-Week 73 >=140	0	0	0	0
Ferritin-Week 85 <140	0	1	1	2
Ferritin-Week 85 >=140	0	0	0	0
%Transferrin Saturation - Baseline <45	15	20	18	53
%Transferrin Saturation Baseline 45 - <50	3	0	1	4
%Transferrin Saturation Baseline 50 - <69	0	0	1	1
%Transferrin Saturation Baseline >=69	0	0	0	0
%Transferrin Saturation Week 13 <45	12	15	13	40
%Transferrin Saturation Week 13 45 - <50	1	0	1	2
%Transferrin Saturation Week 13 50 - <69	2	1	2	5

%Transferrin Saturation Week 13 >=69	0	0	0	0
%Transferrin Saturation Week 25 <45	9	10	9	28
%Transferrin Saturation Week 25 45 - <50	0	1	2	3
%Transferrin Saturation Week 25 50 - <69	1	1	2	4
%Transferrin Saturation Week 25 >=69	0	0	0	0
%Transferrin Saturation Week 37 <45	4	6	11	21
%Transferrin Saturation Week 37 45 - <50	1	0	0	1
%Transferrin Saturation Week 37 50 - <69	1	1	1	3
%Transferrin Saturation Week 37 >=69	0	0	0	0
%Transferrin Saturation Week49 <45	6	4	6	16
%Transferrin Saturation Week 49 45 - <50	0	0	1	1
%Transferrin Saturation Week 49 50 - <69	1	2	1	4
%Transferrin Saturation Week 49 >=69	0	0	0	0
%Transferrin Saturation Week 61 <45	1	2	3	6
%Transferrin Saturation Week61 45 - <50	0	1	0	1
%Transferrin Saturation Week 61 50 - <69	0	0	0	0
%Transferrin Saturation Week 61 >=69	0	0	0	0
%Transferrin Saturation Week 73 <45	2	1	2	5
%Transferrin Saturation Week 73 45 - <50	0	1	0	1
%Transferrin Saturation Week 73 50 - <69	0	0	0	0
%Transferrin Saturation Week 73 >=69	0	0	0	0
%Transferrin Saturation Week 85 <45	0	1	1	2
%Transferrin Saturation Week 85 45 - <50	0	0	0	0
%Transferrin Saturation Week 85 50 - <69	0	0	0	0
%Transferrin Saturation Week85 >=69	0	0	0	0

Notes:

[22] - Not all subjects had evaluable data at each category

[23] - Not all subjects had evaluable data at each category

[24] - Not all subjects had evaluable data at each category

[25] - Not all subjects had evaluable data at each category

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Significant Results of Physical Examinations Including Nose and Throat Mucosal Examinations

End point title	Number of Subjects with Significant Results of Physical Examinations Including Nose and Throat Mucosal Examinations[26]

End point description:

Physical examinations were conducted by a physician, trained physician's assistant, or nurse practitioner as acceptable according to local regulation. A targeted nose and throat mucosal exam was performed to monitor for any signs of mucosal telangiectasias. The clinically significant physical examination results were determined by the investigator.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose

of study medication.

End point type	Primary

End point timeframe:

2 Years

Notes:

[26] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Tanner Stage

End point title	Summary of Tanner Stage[27]

End point description:

Determination of Tanner stage to monitor for signs of accelerated sexual development were conducted by a physician, trained physician's assistant or nurse practitioner as acceptable according to local regulation.
The physical changes in pubertal development (pubic hair, penis and testes) were assessed using the system described by Marshall and Tanner. More details about the system can be referred from Tanner JM. Growth at Adolescence. Blackwell Scientific Publications 1962; 2nd edition.
Subject's Week 97 visit within study B5161002 (parent study) was collected as screening data. Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. N represents the corresponding number of evaluable subjects in each arm where not all subjects were analyzed. N=x,y,z,t in the following table represents the number of evaluable subjects in Sequence groups 1,2,3 and Total.

End point type	Primary

End point timeframe:

Screening, Baseline, Week 49. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

Notes:

[27] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
Public Hair, NotDetected(ND) Screening (N=1,1,0,2)	0	1	0	1
Public Hair, Stage 1, Screening (N=1,1,0,2)	1	0	0	1
Public Hair, Stage 2, Screening (N=1,1,0,2)	0	0	0	0
Public Hair, Stage 3, Screening (N=1,1,0,2)	0	0	0	0

Public Hair, Stage 4, Screening (N=1,1,0,2)	0	0	0	0
Public Hair, Stage 5, Screening (N=1,1,0,2)	0	0	0	0
Public Hair, ND, Baseline	1	0	0	1
Public Hair, Stage 1, Baseline	12	9	12	33
Public Hair, Stage 2, Baseline	5	10	8	23
Public Hair, Stage 3, Baseline	1	1	0	2
Public Hair, Stage 4, Baseline	0	0	0	0
Public Hair, Stage 5, Baseline	0	0	0	0
Public Hair, ND/NA, Week 49 (N=7,6,8,21)	0	0	0	0
Public Hair, Stage 1, Week 49 (N=7,6,8,21)	3	3	5	11
Public Hair, Stage 2 Week 49 (N=7,6,8,21)	4	3	3	10
Public Hair, Stage 3, Week 49 (N=7,6,8,21)	0	0	0	0
Public Hair, Stage 4, Week 49 (N=7,6,8,21)	0	0	0	0
Public Hair, Stage 5, Week 49 (N=7,6,8,21)	0	0	0	0
Penis, ND, Screening (N=1, 1, 0, 2)	0	1	0	1
Penis, Stage 1, Screening (N=1, 1, 0, 2)	1	0	0	1
Penis, Stage 2, Screening (N=1, 1, 0, 2)	0	0	0	0
Penis, Stage 3, Screening (N=1, 1, 0, 2)	0	0	0	0
Penis, Stage 4, Screening (N=1, 1, 0, 2)	0	0	0	0
Penis, Stage 5, Screening (N=1, 1, 0, 2)	0	0	0	0
Penis, ND / NA, Baseline	1	0	0	1
Penis, Stage 1, Baseline	13	11	11	35
Penis, Stage 2, Baseline	5	9	9	23
Penis, Stage 3, Baseline	0	0	0	0
Penis, Stage 4, Baseline	0	0	0	0
Penis, Stage 5, Baseline	0	0	0	0
Penis, ND, Week 49 (N=7,6,8,21)	0	0	0	0
Penis, Stage 1, Week 49 (N=7,6,8,21)	4	2	4	10
Penis, Stage 2, Week 49 (N=7,6,8,21)	3	4	3	10
Penis, Stage 3, Week 49 (N=7,6,8,21)	0	0	1	1
Penis, Stage 4, Week 49 (N=7,6,8,21)	0	0	0	0
Penis, Stage 5, Week 49 (N=7,6,8,21)	0	0	0	0
Testes, ND, Screening (N=1, 1, 0, 2)	0	1	0	1
Testes, Stage 1, Screening (N=1, 1, 0, 2)	1	0	0	1
Testes, Stage 2, Screening (N=1, 1, 0, 2)	0	0	0	0
Testes, Stage 3, Screening (N=1, 1, 0, 2)	0	0	0	0
Testes, Stage 4, Screening (N=1, 1, 0, 2)	0	0	0	0
Testes, Stage 5, Screening (N=1, 1, 0, 2)	0	0	0	0
Testes, ND, Baseline	1	0	0	1
Testes, Stage 1, Baseline	13	10	10	33
Testes, Stage 2, Baseline	5	9	10	24
Testes, Stage 3, Baseline	0	1	0	1
Testes, Stage 4, Baseline	0	0	0	0

Testes, Stage 5, Baseline	0	0	0	0
Testes, ND, Week 49 (N=7,6,8,21)	0	0	0	0
Testes, Stage 1, Week 49 (N=7,6,8,21)	4	4	1	9
Testes, Stage 2, Week 49 (N=7,6,8,21)	3	2	6	11
Testes, Stage 3, Week 49 (N=7,6,8,21)	0	0	1	1
Testes, Stage 4, Week 49 (N=7,6,8,21)	0	0	0	0
Testes, Stage 5, Week 49 (N=7,6,8,21)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Testicular Volume

End point title	Summary of Testicular Volume[28]

End point description:

Testicular volume was used to monitor pubertal development. Subject's Week 97 visit within Study B5161002 (parent study) was collected as screening data in current study. Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. N=x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Primary

End point timeframe:

Screening, Baseline, Week 49. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

Notes:

[28] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	18[29]	20[30]	20[31]	58[32]
Units: Milliliter				
arithmetic mean (standard deviation)				
Left Testis Volume - Screening (N=1, 0, 0, 1)	3.0 (± 99999)	99999 (± 99999)	99999 (± 99999)	3.0 (± 99999)
Left Testis Volume - Baseline (N=18, 20, 20, 58)	2.7 (± 1.07)	2.8 (± 1.06)	2.7 (± 1.63)	2.7 (± 1.27)
Left Testis Volume - Week 49 (N=7, 6, 8, 21)	2.6 (± 0.98)	2.5 (± 0.55)	3.8 (± 3.41)	3.0 (± 2.19)
Right Testis Volume - Screening (N=1, 0, 0, 1)	3.0 (± 99999)	99999 (± 99999)	99999 (± 99999)	3.0 (± 99999)
Right Testis Volume - Baseline (N=18, 20, 20, 58)	2.7 (± 1.03)	2.8 (± 0.97)	2.6 (± 1.64)	2.7 (± 1.23)
Right Testis Volume - Week 49 (N=7, 6, 8, 21)	2.6 (± 0.98)	2.5 (± 0.55)	3.6 (± 3.46)	3.0 (± 2.20)

Notes:

[29] - If no evaluable data collected, 99999 was entered instead.

[30] - If no evaluable data collected, 99999 was entered instead.

[31] - If no evaluable data collected, 99999 was entered instead.

[32] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Post-Baseline Vital Signs Data Meeting Categorical Summarization Criteria - B5161004 Baseline

End point title	Number of Subjects With Post-Baseline Vital Signs Data Meeting Categorical Summarization Criteria - B5161004 Baseline[33]

End point description:

The number of subjects with data of pre-dose supine blood pressure meeting categorical summarization were recorded in this table. Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication.
Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. (DBP=diastolic blood pressure, SBP=systolic blood pressure; The unit for blood pressure is: mmHg, the unit for pulse rate is: beats per minute [BPM])

End point type	Primary

End point timeframe:

2 Years

Notes:

[33] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[34]	20[35]	20[36]	59
Units: Subjects				
Supine SBP - Observed Values <70+2×Age (2-10years)	1	1	0	2
Supine SBP - Observed Values < 90 (11-17 years)	0	1	1	2
Maximum Increase From Baseline in Supine SBP >=30	1	0	3	4
Maximum Decrease From Baseline in Supine SBP >=30	0	1	0	1
Supine DBP - Observed Values <50 (<18 years)	1	1	2	4
Maximum Increase From Baseline in Supine DBP >=20	3	1	5	9
Maximum Decrease From Baseline in Supine DBP >=20	0	2	0	2
Supine Pulse Rate-Observed Values<40BPM(<18 years)	0	0	0	0
Supine Pulse Rate-Observed Values>120BPM(<18years)	2	0	1	3

Notes:

[34] - Not all subjects had evaluable data at each category

[35] - Not all subjects had evaluable data at each category

[36] - Not all subjects had evaluable data at each category

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Post-Baseline Vital Signs Data Meeting Categorical Summarization Criteria - Overall Baseline

End point title	Number of Subjects With Post-Baseline Vital Signs Data Meeting Categorical Summarization Criteria - Overall Baseline[37]

End point description:

The number of subjects with data of pre-dose supine blood pressure meeting categorical summarization were recorded in this table.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. Overall Baseline was defined as the last pre-dose assessment prior to the first day of dosing in study B5161002. (DBP=diastolic blood pressure, SBP=systolic blood pressure; The unit for blood pressure is: mmHg).

End point type	Primary

End point timeframe:

2 Years

Notes:

[37] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
Maximum Increase From Baseline in Supine SBP >=30	2	6	2	10
Maximum Decrease From Baseline in Supine SBP >=30	0	3	4	7
Maximum Increase From Baseline in Supine DBP >=20	8	8	10	26
Maximum Decrease From Baseline in Supine DBP >=20	4	4	8	16

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Post-Baseline ECG Data Meeting Categorical Summarization Criteria - B5161004 Baseline

End point title	Number of Subjects With Post-Baseline ECG Data Meeting Categorical Summarization Criteria - B5161004 Baseline[38]

End point description:

QTcF=QT/(60/Hour)**(1/3). Means of replicates were used in the calculations.
QT=time between the start of the Q wave and the end of the T wave in the heart's electrical cycle; QTcF=corrected QT (Fridericia correction). All scheduled ECGs were performed after the subject had rested quietly for at least 10 minutes in a supine position.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. Baseline was defined as the average of the last triplicate pre-dose measurements prior to Day 1 in B5161004.

End point type	Primary

End point timeframe:

2 Years

Notes:

[38] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	18	20	20	58
Units: Subjects				
Maximum(Max)QTcF Interval-ObservedValues<450msec	18	20	18	56
Max QTcF Interval -Observed Values450-<480msec	0	0	2	2
Max QTcF Interval -Observed Values480-<500msec	0	0	0	0
Max QTcF Interval -Observed Values>=500msec	0	0	0	0
Max QTcF Interval Increase From Baseline<30msec	16	20	18	54
Max QTcF Interval Increase From Baseline30-<60msec	2	0	0	2
Max QTcF Interval Increase From Baseline>= 60msec	0	0	2	2

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Post-Baseline ECG Data Meeting Categorical Summarization Criteria - Overall Baseline

End point title	Number of Subjects With Post-Baseline ECG Data Meeting Categorical Summarization Criteria - Overall Baseline[39]

End point description:

QT=time between the start of the Q wave and the end of the T wave in the heart's electrical cycle; QTcF=corrected QT (Fridericia correction). All scheduled ECGs were performed after the subject had rested quietly for at least 10 minutes in a supine position.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. Overall baseline was defined as the average of the last triplicate pre-dose measurements prior to the first day of dosing in study B5161002.

End point type	Primary

End point timeframe:

2 Years

Notes:

[39] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
Maximum QTcF Interval Increase From Baseline <30	11	15	17	43
Max-QTcF Interval IncreaseFromBaseline30-<60msec	7	5	1	13
Maximum QTcF Interval Increase From Baseline >=60	1	0	2	3

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Iron Accumulation Data Meeting Categorical Summarization Criteria

End point title	Number of Subjects With Iron Accumulation Data Meeting Categorical Summarization Criteria[40]

End point description:

Liver Magnetic Resonance Imaging (MRIs) were sent to an independent central radiology imaging facility for calculation of the average R2* value which was used to monitor for iron accumulation in the liver. Mean R2* values had been used in the calculations.
Normal: R2* <= 75 Hz at 1.5 T or <=139 Hz at 3.0 T; Above Normal: R2* > 75 Hz and <= 190 Hz at 1.5 T or R2* > 139 Hz and <= 369 Hz at 3.0 T
Mild overload: R2* > 190 Hz at 1.5 T or R2* > 369 Hz at 3.0 T
Data from Subject's Week 93 visit in Study B5161002 (parent study) were used for screening in the current study. Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. N=x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Primary

End point timeframe:

Screening and Week 49. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

Notes:

[40] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
Screening - Normal (N=19, 20, 20, 59)	19	20	20	59
Screening - Above Normal (N=19, 20, 20, 59)	0	0	0	0
Screening - Mild Overload (N=19, 20, 20, 59)	0	0	0	0
Week 49 - Normal (N=7, 6, 8, 21)	7	6	8	21
Week 49 - Above Normal (N=7, 6, 8, 21)	0	0	0	0
Week 49 - Mild Overload (N=7, 6, 8, 21)	0	0	0	0
Total - Normal (N=19, 20, 20, 59)	19	20	20	59
Total - Above Normal (N=19, 20, 20, 59)	0	0	0	0
Total - Mild Overload (N=19, 20, 20, 59)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Left Ventricular Ejection Fraction (LVEF) by Cardiac MRI - B5161004 Baseline

End point title	Change From Baseline in Left Ventricular Ejection Fraction (LVEF) by Cardiac MRI - B5161004 Baseline[41]

End point description:

LVEF was measured by cardiac magnetic resonance imaging (MRI) or echocardiography. The same method of cardiac imaging was used consistently for each subject. Cardiac MRIs were read by a central imaging vendor, while echocardiograms were read locally (at each site). The table presents the results from cardiac MRIs.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. N=x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Primary

End point timeframe:

Baseline and Week 49. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

Notes:

[41] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[42]	20[43]	20	59
Units: Percentage				
arithmetic mean (standard deviation)				
Baseline - Observed Values (N=2, 4, 5, 11)	56.000 (± 5.6569)	60.750 (± 2.2174)	62.400 (± 5.6833)	60.636 (± 4.8430)
Week 49 - Observed Values (N=1, 0, 2, 3)	57.000 (± 99999)	99999 (± 99999)	67.000 (± 4.2426)	63.667 (± 6.5064)
Week 49 - Change From Baseline (N=1, 0, 2, 3)	-3.000 (± 99999)	99999 (± 99999)	-1.500 (± 4.9497)	-2.000 (± 3.6056)

Notes:

[42] - If no evaluable data collected, 99999 was entered instead.

[43] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Left Ventricular Ejection Fraction (LVEF) by Cardiac MRI - Overall Baseline

End point title	Change From Baseline in Left Ventricular Ejection Fraction (LVEF) by Cardiac MRI - Overall Baseline[44]

End point description:

LVEF was measured by cardiac magnetic resonance imaging (MRI) or echocardiography. The same method of cardiac imaging was used consistently for each subject. Cardiac MRIs were read by a central imaging vendor, while echocardiograms were read locally (at each site). The table presents the results from cardiac MRIs.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Primary

End point timeframe:

Baseline, Weeks 49, 97, 146. Overall baseline was defined as the last pre-dose assessment prior to the first day of dosing in study B5161002. Week 1 was counted starting from the study treatment in study B5161002.

Notes:

[44] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[45]	20[46]	20	59
Units: Percentage				
arithmetic mean (standard deviation)				
Baseline - Observed Values (N = 2, 4, 6, 12)	66.000 (± 8.4853)	61.250 (± 3.5000)	61.333 (± 5.3541)	62.083 (± 5.1250)
Week 49 - Observed Values (N = 2, 4, 5, 11)	55.000 (± 11.3137)	57.750 (± 4.1130)	63.200 (± 5.4498)	59.727 (± 6.4667)
Week 49 - Change From Baseline (N = 2, 4, 5, 11)	-11.000 (± 2.8284)	-3.500 (± 1.9149)	0.000 (± 7.4498)	-3.273 (± 6.4357)
Week 97 - Observed Values (N = 2, 4, 5, 11)	56.000 (± 5.6569)	60.750 (± 2.2174)	62.400 (± 5.6833)	60.636 (± 4.8430)
Week 97 - Change From Baseline (N = 2, 4, 5, 11)	-10.000 (± 2.8284)	-0.500 (± 2.8868)	-0.800 (± 6.5727)	-2.364 (± 5.9038)
Week 146 - Observed Values (N = 1, 0, 2, 3)	57.000 (± 99999)	99999 (± 99999)	67.000 (± 4.2426)	63.667 (± 6.5064)
Week 146 - Change From Baseline (N = 1, 0, 2, 3)	-15.000 (± 99999)	99999 (± 99999)	3.500 (± 0.7071)	-2.667 (± 10.6927)

Notes:

[45] - If no evaluable data collected, 99999 was entered instead.

[46] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Left Ventricular Ejection Fraction (LVEF) by Echocardiogram - B5161004 Baseline

End point title	Change From Baseline in Left Ventricular Ejection Fraction (LVEF) by Echocardiogram - B5161004 Baseline[47]

End point description:

LVEF was measured by cardiac magnetic resonance imaging (MRI) or echocardiography. The same method of cardiac imaging was used consistently for each subject. Cardiac MRIs were read by a central imaging vendor, while echocardiograms were read locally (at each site). The table presents the results from echocardiograms.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. N=x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Primary

End point timeframe:

Baseline, Week 49. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

Notes:

[47] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Percentage				
arithmetic mean (standard deviation)				
Baseline - Observed Values (N=17, 17, 14, 48)	60.359 (± 3.7545)	62.461 (± 6.0180)	62.543 (± 5.3731)	61.740 (± 5.1170)
Week 49 - Observed Values (N=5, 6, 5, 16)	62.060 (± 6.4972)	61.350 (± 5.1122)	62.300 (± 6.6656)	61.869 (± 5.6567)
Week 49 - Change From Baseline (N=5, 6, 5, 16)	-0.400 (± 5.0334)	-3.900 (± 8.9252)	2.200 (± 7.6056)	-0.900 (± 7.4580)

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Left Ventricular Ejection Fraction (LVEF) by Echocardiogram - Overall Baseline

End point title	Change From Baseline in Left Ventricular Ejection Fraction (LVEF) by Echocardiogram - Overall Baseline[48]

End point description:

LVEF was measured by cardiac magnetic resonance imaging (MRI) or echocardiography. The same method of cardiac imaging was used consistently for each subject. Cardiac MRIs were read by a central imaging vendor, while echocardiograms were read locally (at each site). The table presents the results from echocardiograms.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. N=x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Primary

End point timeframe:

Baseline, Weeks 49, 97, 146. Overall baseline was defined as the last pre-dose assessment prior to the first day of dosing in study B5161002. Week 1 was counted starting from the study treatment in study B5161002.

Notes:

[48] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Percentage				
arithmetic mean (standard deviation)				
Baseline - Observed Values (N=17,16,15,48)	63.288 (± 4.3743)	64.094 (± 4.3025)	64.073 (± 4.5848)	63.802 (± 4.3395)
Week 49 - Observed Values (N=17,15,15,47)	63.118 (± 4.6038)	63.060 (± 5.5516)	63.860 (± 4.7891)	63.336 (± 4.8851)
Week 49 - Change From Baseline (N=17,15,15,47)	-0.171 (± 5.7432)	-1.040 (± 4.8861)	-0.213 (± 6.1487)	-0.462 (± 5.5142)
Week 97 - Observed Values (N=17,16,14,47)	60.359 (± 3.7545)	62.284 (± 6.1693)	62.543 (± 5.3731)	61.665 (± 5.1450)
Week 97 - Change From Baseline (N=17,16,14,47)	-2.929 (± 5.4060)	-1.810 (± 6.1321)	-1.414 (± 6.4799)	-2.097 (± 5.8924)
Week 146 - Observed Values (N=5,6,5,16)	62.060 (± 6.4972)	61.350 (± 5.1122)	62.300 (± 6.6656)	61.869 (± 5.6567)

Week 146 - Change From Baseline (N=5,6,5,16)	-1.240 (± 2.3416)	-4.833 (± 4.2151)	-1.440 (± 11.6993)	-2.650 (± 6.8514)

Statistical analyses

No statistical analyses for this end point

Primary: Bone Age to Chronological Age Ratio

End point title	Bone Age to Chronological Age Ratio[49]

End point description:

Bone age assessment was evaluated by the ratio of the bone age to the chronological age using the X rays of the hand and wrist. Ratio of bone age to chronological age was calculated by bone age/chronological age at scan date. Chronological age at scan date was calculated by (scan date-date of birth+1)/365.25.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Primary

End point timeframe:

Baseline and Week 49. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

Notes:

[49] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Ratio				
arithmetic mean (standard deviation)				
Baseline (N = 19, 20, 20, 59)	0.76 (± 0.213)	0.74 (± 0.195)	0.81 (± 0.177)	0.77 (± 0.194)
Week 49 (N = 7, 6, 7, 20)	0.74 (± 0.197)	0.65 (± 0.157)	0.70 (± 0.172)	0.70 (± 0.172)

Statistical analyses

No statistical analyses for this end point

Primary: Whole Body and Spine DXA: Bone Mineral Density Z-Score, Height Adjusted Over Time

End point title	Whole Body and Spine DXA: Bone Mineral Density Z-Score, Height Adjusted Over Time[50]

End point description:

Bone mineral density was monitored by dual energy x-ray absorptiometry (DXA). DXA scans were obtained to evaluate bone mineral density of the spine and whole body without head.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Screening (Week 97 visit within parent study B5161002) and Week 49

Notes:

[50] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[51]	20[52]	20[53]	59[54]
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Spine Total L1 to L4-Screening	-0.687659 (± 0.9152662)	-0.587384 (± 1.0241266)	-0.561789 (± 1.0285799)	-0.613225 (± 0.9731687)
Spine Total L1 to L4 -Week49	-0.131374 (± 0.9251749)	-0.435384 (± 0.5747293)	-0.152854 (± 1.7877768)	-0.227106 (± 1.1053887)
Body Without Head - Screening	-1.936367 (± 1.1544544)	-1.956332 (± 1.3561294)	-1.872619 (± 1.4843432)	-1.921525 (± 1.3187696)
Body Without Head - Week 49	-1.789347 (± 1.1738270)	-1.943538 (± 1.6839551)	-1.455670 (± 1.5655008)	-1.732667 (± 1.4033563)

Notes:

[51] - Not all subjects had evaluable data at each category

[52] - Not all subjects had evaluable data at each category

[53] - Not all subjects had evaluable data at each category

[54] - Not all subjects had evaluable data at each category

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Significant Results of Columbia-Suicide Severity Rating Scale (C-SSRS) Assessment

End point title	Number of Subjects with Significant Results of Columbia-Suicide Severity Rating Scale (C-SSRS) Assessment[55]

End point description:

C-SSRS was conducted with the subject's caregiver/legal guardian on the subject's behalf throughout the study, rather than administering this evaluation directly with the study subjects. If at any visit the subject endorsed a 4 or 5 on the C-SSRS ideation section or reported any suicidality behavior, then an evaluation of suicide risk (risk assessment) had to be completed and the subject must have been discontinued.
Analysis population was the Safety Analysis Set consisting of subjects who had received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

2 Years

Notes:

[55] - 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 planned for this endpoint

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the 4 Stair Climb (4SC) - B5161004 Baseline

End point title	Change From Baseline on the 4 Stair Climb (4SC) - B5161004 Baseline

End point description:

The 4SC quantified the time required for a subject to ascend 4 standard steps. The functional assessment of 4SC was conducted by a physiotherapist (or exercise physiologist). In order to provide optimal testing conditions and consistency in endpoint measurements, the functional assessments were completed at approximately the same time of day.
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13, 25, 49, 73. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[56]	20[57]	20[58]	59
Units: Seconds				
arithmetic mean (confidence interval 95%)				
Baseline (N = 15, 13, 11, 39)	7.268 (3.779 to 10.757)	5.218 (3.370 to 7.065)	5.373 (2.936 to 7.809)	6.050 (4.530 to 7.570)
Week 13 (N = 15, 13, 11, 39)	0.839 (-0.680 to 2.357)	0.821 (0.178 to 1.463)	0.400 (-0.416 to 1.216)	0.709 (0.098 to 1.320)
Week 25 (N = 10, 9, 8, 27)	1.248 (-0.050 to 2.546)	0.319 (-0.073 to 0.710)	0.663 (-0.368 to 1.693)	0.765 (0.236 to 1.294)
Week 49 (N = 6, 4, 5, 15)	10.150 (-5.363 to 25.663)	0.998 (-0.140 to 2.135)	2.400 (-2.917 to 7.717)	5.126 (-0.460 to 10.712)
Week 73 (N = 2, 2, 1, 5)	9.350 (-99999 to 99999)	3.100 (-99999 to 99999)	1.000 (-99999 to 99999)	5.180 (-0.234 to 10.594)

Notes:

[56] - If no evaluable data collected, 99999 was entered instead.

[57] - If no evaluable data collected, 99999 was entered instead.

[58] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the 4SC - Overall Baseline

End point title	Change From Baseline on the 4SC - Overall Baseline

End point description:

The 4SC quantified the time required for a subject to ascend 4 standard steps. The functional assessment of 4SC was conducted by a physiotherapist (or exercise physiologist). In order to provide optimal testing conditions and consistency in endpoint measurements, the functional assessments were completed at approximately the same time of day.
This is the overall change from baseline which included the change since enrolling in the parent study B5161002.
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 9,17,25,33,41,49,57,65,73,81,89,97,110,122,146,170. Overall baseline was defined as the last pre-dose assessment prior to the first day of dosing in study B5161002. Week 1 was counted starting from the study treatment in study B5161002.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[59]	20[60]	20[61]	59
Units: Seconds				
arithmetic mean (confidence interval 95%)				
Baseline (N = 19, 20, 20, 59)	4.381 (3.442 to 5.319)	5.664 (3.728 to 7.599)	5.717 (4.141 to 7.292)	5.268 (4.409 to 6.128)
Week 9 (N = 19, 19, 20, 58)	-0.096 (-0.582 to 0.389)	0.898 (-0.444 to 2.240)	0.879 (0.103 to 1.654)	0.566 (0.046 to 1.085)
Week 17 (N = 19, 17, 19, 55)	0.500 (-0.365 to 1.365)	2.270 (-0.898 to 5.438)	1.493 (0.009 to 2.977)	1.390 (0.309 to 2.472)
Week 25 (N = 18, 18, 17, 53)	0.427 (-0.385 to 1.239)	2.835 (0.094 to 5.576)	2.836 (-0.775 to 6.447)	2.018 (0.577 to 3.458)
Week 33 (N = 18, 18, 17, 53)	1.298 (-1.043 to 3.639)	3.713 (-0.573 to 7.999)	1.804 (0.151 to 3.457)	2.280 (0.630 to 3.930)
Week 41 (N = 18, 17, 16, 51)	0.920 (-0.665 to 2.505)	3.361 (-1.170 to 7.892)	2.217 (0.192 to 4.241)	2.140 (0.508 to 3.773)
Week 49 (N = 17, 16, 16, 49)	0.480 (-0.040 to 1.000)	2.391 (0.151 to 4.630)	1.898 (0.397 to 3.399)	1.567 (0.704 to 2.430)
Week 57 (N = 17, 16, 14, 47)	0.712 (0.129 to 1.294)	3.827 (-0.137 to 7.791)	2.914 (-0.289 to 6.118)	2.428 (0.846 to 4.010)
Week 65 (N = 17, 16, 12, 45)	1.337 (0.141 to 2.533)	4.259 (0.138 to 8.380)	2.181 (-1.064 to 5.426)	2.601 (0.941 to 4.261)
Week 73 (N = 16, 15, 14, 45)	1.561 (0.066 to 3.055)	3.082 (0.752 to 5.412)	1.849 (0.178 to 3.520)	2.157 (1.150 to 3.164)
Week 81 (N = 16, 14, 14, 44)	1.633 (0.561 to 2.704)	3.006 (-0.084 to 6.096)	2.262 (-0.026 to 4.550)	2.270 (1.087 to 3.453)
Week 89 (N = 17, 13, 13, 43)	1.687 (0.680 to 2.694)	2.069 (0.779 to 3.359)	3.182 (-0.296 to 6.661)	2.255 (1.161 to 3.349)
Week 97 (N = 17, 13, 13, 43)	2.652 (0.323 to 4.981)	1.874 (0.562 to 3.185)	1.790 (0.217 to 3.363)	2.156 (1.123 to 3.189)
Week 110 (N = 15, 13, 11, 39)	3.811 (0.071 to 7.552)	2.748 (0.950 to 4.547)	1.806 (-0.435 to 4.048)	2.892 (1.330 to 4.453)
Week 122 (N = 10, 9, 8, 27)	3.128 (0.653 to 5.603)	1.781 (0.760 to 2.802)	1.909 (-0.412 to 4.229)	2.318 (1.259 to 3.377)
Week 146 (N = 6, 4, 5, 15)	11.933 (-4.591 to 28.458)	2.498 (-1.975 to 6.970)	4.034 (-3.016 to 11.084)	6.784 (0.749 to 12.819)

Week 170 (N = 2, 2, 1, 5)	10.450 (-99999 to 99999)	6.150 (-99999 to 99999)	2.100 (-99999 to 99999)	7.060 (1.542 to 12.578)

Notes:

[59] - If no evaluable data collected, 99999 was entered instead.

[60] - If no evaluable data collected, 99999 was entered instead.

[61] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Forced Vital Capacity (FVC) - B5161004 Baseline

End point title	Change From Baseline on the Forced Vital Capacity (FVC) - B5161004 Baseline

End point description:

FVC was measured using the FVC maneuver by spirometry to evaluate respiratory muscle function. The best (largest) FVC measurement from a set of 3 was captured on the database.
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13, 25, 49 and 73. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[62]	20[63]	20[64]	59
Units: Litre				
arithmetic mean (confidence interval 95%)				
Baseline (N = 16, 17, 18, 51)	1.6550 (1.4829 to 1.8271)	1.7029 (1.4607 to 1.9452)	1.8678 (1.6245 to 2.1110)	1.7461 (1.6227 to 1.8694)
Week 13 (N = 16, 16, 15, 47)	0.0344 (-0.0355 to 0.1042)	0.1106 (-0.0620 to 0.2832)	0.0380 (-0.0417 to 0.1177)	0.0615 (-0.0024 to 0.1254)
Week 25 (N = 11, 12, 14, 37)	0.0718 (-0.0701 to 0.2137)	0.1467 (0.0081 to 0.2852)	0.1086 (-0.0094 to 0.2266)	0.1100 (0.0409 to 0.1791)
Week 49 (N = 7, 6, 7, 20)	0.2086 (0.0862 to 0.3310)	0.2633 (-0.0621 to 0.5887)	0.0671 (-0.0385 to 0.1728)	0.1755 (0.0794 to 0.2716)
Week 73 (N = 2, 2, 2, 6)	0.2800 (-99999 to 99999)	0.3750 (-99999 to 99999)	0.1450 (-99999 to 99999)	0.2667 (-0.0373 to 0.5707)

Notes:

[62] - If no evaluable data collected, 99999 was entered instead.

[63] - If no evaluable data collected, 99999 was entered instead.

[64] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the FVC - Overall Baseline

End point title	Change From Baseline on the FVC - Overall Baseline

End point description:

Forced vital capacity (FVC) was measured using the FVC maneuver by spirometry to evaluate respiratory muscle function. The best (largest) FVC measurement from a set of 3 was captured on the database. This is the overall change from baseline which included the change since enrolling in the parent study B5161002.
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 9,17,25,33,41,49,57,65,73,81,89,97,110,122,146,170. Overall baseline was defined as the last pre-dose assessment prior to the first day of dosing in study B5161002. Week 1 was counted starting from the study treatment in study B5161002.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[65]	20[66]	20[67]	59
Units: Litre				
arithmetic mean (confidence interval 95%)				
Baseline (N = 19, 20, 20, 59)	1.3753 (1.2305 to 1.5200)	1.5810 (1.4256 to 1.7364)	1.6265 (1.4322 to 1.8208)	1.5302 (1.4353 to 1.6250)
Week 9 (N = 19, 19, 20, 58)	0.1205 (0.0093 to 0.2317)	0.1089 (-0.0307 to 0.2486)	-0.0435 (-0.1331 to 0.0461)	0.0602 (-0.0049 to 0.1253)
Week 17 (N = 19, 20, 20, 59)	0.0837 (-0.0234 to 0.1907)	0.0700 (-0.0113 to 0.1513)	0.0585 (-0.0097 to 0.1267)	0.0705 (0.0237 to 0.1173)
Week 25 (N = 19, 20, 20, 59)	0.0679 (-0.0461 to 0.1819)	0.1140 (0.0204 to 0.2076)	-0.0135 (-0.1276 to 0.1006)	0.0559 (-0.0040 to 0.1158)
Weed 33 (N = 19, 20, 20, 59)	0.1463 (0.0379 to 0.2548)	0.0740 (-0.0414 to 0.1894)	0.1100 (0.0425 to 0.1775)	0.1095 (0.0553 to 0.1637)
Week 41 (N = 19, 20, 20, 59)	0.1484 (0.0343 to 0.2625)	0.1115 (-0.0298 to 0.2528)	0.1320 (0.0582 to 0.2058)	0.1303 (0.0689 to 0.1918)
Week 49 (N = 18, 20, 20, 58)	0.1328 (-0.0053 to 0.2709)	0.1350 (0.0427 to 0.2273)	0.1565 (0.1011 to 0.2119)	0.1417 (0.0886 to 0.1948)
Week 57 (N = 19, 20, 18, 57)	0.1063 (-0.0470 to 0.2597)	0.1735 (0.0607 to 0.2863)	0.1656 (0.0406 to 0.2905)	0.1486 (0.0772 to 0.2200)
Week 65 (N = 19, 20, 19, 58)	0.2005 (0.0530 to 0.3480)	0.1830 (0.0959 to 0.2701)	0.1726 (0.0647 to 0.2806)	0.1853 (0.1225 to 0.2482)
Week 73 (N = 18, 20, 20, 58)	0.1706 (-0.0177 to 0.3588)	0.1925 (0.0706 to 0.3144)	0.1330 (0.0521 to 0.2139)	0.1652 (0.0927 to 0.2376)
Week 81 (N = 19, 19, 20, 58)	0.2263 (0.0718 to 0.3808)	0.1353 (0.0110 to 0.2595)	0.2045 (0.1279 to 0.2811)	0.1890 (0.1225 to 0.2554)

Week 89 (N = 17, 20, 20, 57)	0.2406 (0.0674 to 0.4137)	0.1960 (0.0389 to 0.3531)	0.2145 (0.1087 to 0.3203)	0.2158 (0.1369 to 0.2946)
Week 97 (N = 19, 20, 20, 59)	0.2932 (0.1616 to 0.4247)	0.1365 (-0.0336 to 0.3066)	0.2375 (0.1472 to 0.3278)	0.2212 (0.1462 to 0.2962)
Week 110 (N = 16, 16, 15, 47)	0.2781 (0.1373 to 0.4189)	0.2256 (0.0736 to 0.3777)	0.2407 (0.1167 to 0.3646)	0.2483 (0.1734 to 0.3232)
Week 122 (N = 11, 12, 14, 37)	0.2973 (0.0532 to 0.5413)	0.3708 (0.2666 to 0.4750)	0.3221 (0.1436 to 0.5007)	0.3305 (0.2360 to 0.4250)
Week 146 (N = 7, 6, 7, 20)	0.4629 (0.1599 to 0.7658)	0.4167 (0.1726 to 0.6607)	0.3114 (0.1531 to 0.4698)	0.3960 (0.2797 to 0.5123)
Week 170 (N = 2, 2, 2, 6)	0.5500 (-99999 to 99999)	0.2850 (-99999 to 99999)	0.4900 (-99999 to 99999)	0.4417 (0.1950 to 0.6884)

Notes:

[65] - If no evaluable data collected, 99999 was entered instead.

[66] - If no evaluable data collected, 99999 was entered instead.

[67] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Northstar Ambulatory Assessment (NSAA) Score - B5161004 Baseline

End point title	Change From Baseline on the Northstar Ambulatory Assessment (NSAA) Score - B5161004 Baseline

End point description:

The NSAA was a 17-item test that measured gross motor function. Each individual item was evaluated with either 0-unable to perform independently, 1-able to perform with assistance, 2-able to perform without assistance. A total score was achieved by summing all the individual items. The total score could range from 0 to 34 (fully-independent function).
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13, 25, 49, 73. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[68]	20[69]	20[70]	59
Units: Units on a Scale				
arithmetic mean (confidence interval 95%)				
Baseline (N = 15, 17, 17, 49)	16.4 (11.8 to 21.0)	17.1 (11.6 to 22.6)	12.9 (6.9 to 19.0)	15.4 (12.5 to 18.4)
Week 13 (N = 15, 17, 16, 48)	-0.6 (-1.3 to 0.1)	-1.7 (-3.0 to -0.4)	-0.4 (-1.6 to 0.7)	-0.9 (-1.5 to -0.3)
Week 25 (N = 10, 12, 13, 35)	-1.8 (-3.1 to -0.5)	-0.7 (-1.6 to 0.2)	-0.8 (-2.0 to 0.5)	-1.0 (-1.7 to -0.4)

Week 49 (N = 7, 6, 6, 19)	-3.6 (-6.9 to -0.2)	-3.2 (-5.8 to -0.6)	-3.2 (-5.6 to -0.7)	-3.3 (-4.6 to -2.0)
Week 73 (N = 2, 2, 2, 6)	-5.5 (-99999 to 99999)	-3.0 (-99999 to 99999)	-4.0 (-99999 to 99999)	-4.2 (-7.4 to -1.0)

Notes:

[68] - If no evaluable data collected, 99999 was entered instead.

[69] - If no evaluable data collected, 99999 was entered instead.

[70] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the NSAA Score - Overall Baseline

End point title	Change From Baseline on the NSAA Score - Overall Baseline

End point description:

The NSAA was a 17-item test that measured gross motor function. Each individual item was evaluated with either 0-unable to perform independently, 1-able to perform with assistance, 2-able to perform without assistance. A total score was achieved by summing all the individual items. The total score could range from 0 to 34 (fully-independent function). This is the overall change from baseline which included the change since enrolling in the parent study B5161002.
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 9,17,25,33,41,49,57,65,73,81,89,97,110,122,146,170. Overall baseline was defined as the last pre-dose assessment prior to the first day of dosing in study B5161002. Week 1 was counted starting from the study treatment in study B5161002.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[71]	20[72]	20[73]	59
Units: Units on a Scale				
arithmetic mean (confidence interval 95%)				
Baseline (N = 19, 20, 20, 59)	20.8 (17.6 to 24.1)	21.2 (17.2 to 25.2)	19.5 (16.0 to 23.0)	20.5 (18.5 to 22.5)
Week 9 (N = 19, 19, 20, 58)	-0.2 (-1.3 to 1.0)	0.4 (-0.6 to 1.4)	-0.8 (-2.4 to 0.8)	-0.2 (-0.9 to 0.5)
Week 17 (N = 19, 20, 19, 58)	0.3 (-1.1 to 1.6)	-2.2 (-5.8 to 1.5)	-0.9 (-2.7 to 0.9)	-0.9 (-2.3 to 0.4)
Week 25 (N = 19, 20, 20, 59)	0.1 (-1.5 to 1.7)	-1.4 (-3.1 to 0.3)	-2.2 (-4.7 to 0.4)	-1.2 (-2.3 to 0.0)
Week 33 (N = 19, 20, 20, 59)	-0.4 (-2.0 to 1.2)	-1.5 (-3.1 to 0.1)	-2.9 (-5.1 to -0.7)	-1.6 (-2.7 to -0.6)
Week 41 (N = 19, 20, 20, 59)	-1.5 (-3.8 to 0.7)	-2.7 (-4.5 to -0.8)	-3.6 (-6.0 to -1.2)	-2.6 (-3.8 to -1.4)
Week 49 (N = 19, 20, 19, 58)	-1.8 (-4.2 to 0.6)	-3.4 (-5.5 to -1.2)	-4.2 (-6.9 to -1.6)	-3.1 (-4.5 to -1.8)
Week 57 (N = 18, 20, 19, 57)	-2.6 (-5.1 to -0.2)	-3.7 (-6.0 to -1.3)	-5.5 (-9.3 to -1.6)	-3.9 (-5.6 to -2.3)
Week 65 (N = 18, 20, 20, 58)	-2.7 (-5.4 to -0.1)	-3.8 (-6.1 to -1.5)	-5.8 (-9.6 to -1.9)	-4.1 (-5.8 to -2.5)

Week 73 (N = 18, 20, 20, 58)	-4.7 (-7.7 to -1.6)	-5.1 (-7.4 to -2.7)	-5.8 (-8.8 to -2.7)	-5.2 (-6.7 to -3.6)
Week 81 (N = 19, 19, 20, 58)	-4.1 (-6.8 to -1.3)	-4.5 (-6.9 to -2.1)	-6.0 (-9.3 to -2.6)	-4.9 (-6.4 to -3.3)
Week 89 (N = 18, 19, 20, 57)	-4.2 (-7.5 to -1.0)	-6.2 (-8.5 to -3.9)	-7.4 (-10.4 to -4.3)	-6.0 (-7.6 to -4.4)
Week 97 (N = 18, 20, 20, 58)	-4.4 (-7.7 to -1.1)	-6.7 (-9.3 to -4.0)	-7.0 (-10.0 to -3.9)	-6.1 (-7.7 to -4.4)
Week 110 (N = 16, 17, 16, 49)	-5.1 (-8.4 to -1.8)	-7.2 (-9.8 to -4.7)	-5.9 (-8.9 to -2.9)	-6.1 (-7.7 to -4.5)
Week 122 (N = 11, 12, 13, 36)	-6.4 (-11.7 to -1.0)	-7.2 (-10.7 to -3.6)	-7.6 (-12.0 to -3.3)	-7.1 (-9.4 to -4.8)
Week 146 (N = 7, 6, 6, 19)	-9.9 (-19.7 to 0.0)	-8.3 (-13.2 to -3.5)	-7.3 (-10.1 to -4.5)	-8.6 (-11.9 to -5.3)
Week 170 (N = 2, 2, 2, 6)	-11.5 (-99999 to 99999)	-12.0 (-99999 to 99999)	-7.0 (-99999 to 99999)	-10.2 (-15.6 to -4.8)

Notes:

[71] - If no evaluable data collected, 99999 was entered instead.

[72] - If no evaluable data collected, 99999 was entered instead.

[73] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the NSAA - Time to Stand From Supine - B5161004 Baseline

End point title	Change From Baseline on the NSAA - Time to Stand From Supine - B5161004 Baseline

End point description:

Rise from supine was a timed functional test within NSAA. This test of time-to-stand from supine was analyzed separately for summary tabulation along with the total NSAA score.
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13, 25, 49, 73. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[74]	20[75]	20[76]	59[77]
Units: Seconds				
arithmetic mean (confidence interval 95%)				
Baseline (N = 6, 11, 8, 25)	4.517 (2.612 to 6.421)	6.508 (3.996 to 9.020)	6.250 (4.552 to 7.948)	5.948 (4.751 to 7.144)
Week 13 (N = 6, 11, 8, 25)	0.330 (-0.231 to 0.891)	1.353 (0.357 to 2.349)	-0.038 (-0.931 to 0.856)	0.662 (0.121 to 1.203)
Week 25 (N = 4, 8, 6, 18)	-0.113 (-0.585 to 0.360)	1.463 (0.315 to 2.610)	-0.167 (-1.410 to 1.076)	0.569 (-0.112 to 1.251)
Week 49 (N = 1, 4, 4, 9)	0.670 (-99999 to 99999)	1.518 (-1.384 to 4.419)	2.978 (-1.944 to 7.899)	2.072 (0.246 to 3.898)

Week 73 (N = 0, 1, 1, 2)	99999 (-99999 to 99999)	10.170 (-99999 to 99999)	2.300 (-99999 to 99999)	6.235 (-99999 to 99999)

Notes:

[74] - If no evaluable data collected, 99999 was entered instead.

[75] - If no evaluable data collected, 99999 was entered instead.

[76] - If no evaluable data collected, 99999 was entered instead.

[77] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the NSAA - Time to Stand From Supine - Overall Baseline

End point title	Change From Baseline on the NSAA - Time to Stand From Supine - Overall Baseline

End point description:

Rise from supine was a timed functional test within NSAA. This test of time-to-stand from supine was analyzed separately for summary tabulation along with the total NSAA score. This is the overall change from baseline which included the change since enrolling in the parent study B5161002.
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 9,17,25,33,41,49,57,65,73,81,89,97,110,122,146,170. Overall baseline was defined as the last pre-dose assessment prior to the first day of dosing in study B5161002. Week 1 was counted starting from the study treatment in study B5161002.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[78]	20[79]	20[80]	59[81]
Units: Seconds				
arithmetic mean (confidence interval 95%)				
Baseline (N = 16, 15, 15, 46)	6.440 (4.446 to 8.434)	7.059 (2.997 to 11.122)	7.046 (5.130 to 8.962)	6.840 (5.348 to 8.331)
Week 9 (N = 16, 14, 12, 42)	-0.140 (-1.049 to 0.769)	0.486 (-0.190 to 1.163)	0.867 (-0.101 to 1.834)	0.356 (-0.116 to 0.829)
Week 17 (N = 16, 12, 13, 41)	10.251 (-11.639 to 32.142)	1.123 (0.185 to 2.060)	1.148 (0.013 to 2.282)	4.693 (-3.384 to 12.770)
Week 25 (N = 16, 12, 10, 38)	1.283 (-0.135 to 2.701)	0.514 (0.055 to 0.973)	1.456 (-0.401 to 3.313)	1.086 (0.364 to 1.808)
Week 33 (N = 15, 12, 11, 38)	1.382 (-0.038 to 2.802)	0.392 (-0.412 to 1.195)	1.143 (-1.200 to 3.485)	1.000 (0.166 to 1.834)
Week 41 (N = 14, 12, 10, 36)	1.184 (0.123 to 2.246)	0.526 (-0.230 to 1.282)	1.620 (-0.213 to 3.453)	1.086 (0.445 to 1.726)
Week 49 (N = 14, 12, 12, 38)	1.642 (-0.005 to 3.289)	0.730 (-0.466 to 1.926)	1.630 (0.269 to 2.991)	1.350 (0.582 to 2.118)
Week 57 (N = 13, 11, 9, 33)	1.577 (-0.212 to 3.366)	1.376 (-0.184 to 2.937)	1.316 (-0.581 to 3.212)	1.439 (0.534 to 2.343)
Week 65 (N = 12, 11, 9, 32)	1.590 (-0.715 to 3.895)	1.570 (-0.113 to 3.253)	1.907 (-0.652 to 4.465)	1.672 (0.556 to 2.788)

Week 73 (N = 12, 11, 11, 34)	2.664 (0.149 to 5.180)	1.765 (0.012 to 3.517)	2.266 (0.410 to 4.123)	2.244 (1.155 to 3.333)
Week 81 (N = 10, 11, 10, 31)	2.153 (-0.046 to 4.352)	2.422 (-0.327 to 5.170)	1.971 (-0.291 to 4.233)	2.190 (0.948 to 3.431)
Week 89 (N = 11, 10, 10, 31)	2.538 (0.479 to 4.598)	3.249 (-1.598 to 8.096)	2.824 (0.109 to 5.539)	2.860 (1.166 to 4.553)
Week 97 (N = 8, 11, 9, 28)	1.009 (-0.440 to 2.458)	2.418 (0.299 to 4.537)	1.933 (0.279 to 3.587)	1.860 (0.896 to 2.823)
Week 110 (N = 6, 11, 9, 26)	0.792 (-0.611 to 2.194)	3.753 (1.266 to 6.239)	2.884 (-0.807 to 6.576)	2.769 (1.226 to 4.311)
Week 122 (N = 4, 8, 6, 18)	-0.133 (-2.124 to 1.859)	4.543 (1.277 to 7.808)	1.750 (-0.120 to 3.620)	2.573 (0.903 to 4.243)
Week 146 (N = 1, 4, 4, 9)	-0.400 (-99999 to 99999)	5.295 (-5.207 to 15.797)	4.978 (-1.086 to 11.041)	4.521 (0.662 to 8.381)
Week 170 (N = 0, 1, 1, 2)	99999 (-99999 to 99999)	13.780 (-99999 to 99999)	4.300 (-99999 to 99999)	9.040 (-99999 to 99999)

Notes:

[78] - If no evaluable data collected, 99999 was entered instead.

[79] - If no evaluable data collected, 99999 was entered instead.

[80] - If no evaluable data collected, 99999 was entered instead.

[81] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the NSAA - Time to Complete 10 m Run/Walk - B5161004 Baseline

End point title	Change From Baseline on the NSAA - Time to Complete 10 m Run/Walk - B5161004 Baseline

End point description:

A time to event analysis was performed for loss of ambulation. Loss of ambulation was defined as the inability to walk unassisted and without braces for at least 10 m, as assessed and reported by the investigator at each study visit, and confirmed by the inability to walk/run 10 m (as 1 component of the NSAA) evaluated at the next visit at which timed function tests were performed.
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13, 25, 49, 73. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[82]	20[83]	20[84]	59
Units: Seconds				
arithmetic mean (confidence interval 95%)				
Baseline (N = 11, 12, 9, 32)	6.245 (4.910 to 7.579)	5.894 (4.694 to 7.094)	5.800 (4.789 to 6.811)	5.988 (5.361 to 6.615)
Week 13 (N = 11, 12, 9, 32)	-0.029 (-0.310 to 0.252)	0.383 (-1.262 to 2.027)	0.089 (-0.195 to 0.372)	0.158 (-0.412 to 0.729)

Week 25 (N = 8, 9, 7, 24)	0.546 (-0.235 to 1.328)	-0.172 (-1.410 to 1.066)	0.743 (-0.231 to 1.717)	0.334 (-0.204 to 0.872)
Week 49 (N = 4, 4, 4, 12)	0.665 (-0.546 to 1.864)	-0.735 (-4.419 to 2.949)	0.488 (-0.822 to 1.797)	0.139 (-0.809 to 1.087)
Week 73 (N = 1, 2, 1, 4)	1.160 (-99999 to 99999)	0.480 (-99999 to 99999)	0.600 (-99999 to 99999)	0.680 (-0.389 to 1.749)

Notes:

[82] - If no evaluable data collected, 99999 was entered instead.

[83] - If no evaluable data collected, 99999 was entered instead.

[84] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the NSAA - Time to Complete 10 m Run/Walk - Overall Baseline

End point title	Change From Baseline on the NSAA - Time to Complete 10 m Run/Walk - Overall Baseline

End point description:

A time to event analysis was performed for loss of ambulation. Loss of ambulation was defined as the inability to walk unassisted and without braces for at least 10 m, as assessed and reported by the investigator at each study visit, and confirmed by the inability to walk/run 10 m (as 1 component of the NSAA) evaluated at the next visit at which timed function tests were performed. This is the overall change from baseline which included the change since enrolling in the parent study B5161002.
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 9,17,25,33,41,49,57,65,73,81,89,97,110,122,146,170. Overall baseline was defined as the last pre-dose assessment prior to the first day of dosing in study B5161002. Week 1 was counted starting from the study treatment in study B5161002.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[85]	20[86]	20[87]	59
Units: Seconds				
arithmetic mean (confidence interval 95%)				
Baseline (N = 19, 18, 18, 55)	5.780 (5.031 to 6.529)	5.862 (5.073 to 6.652)	6.609 (5.596 to 7.623)	6.078 (5.606 to 6.550)
Week 9 (N = 19, 17, 16, 52)	0.159 (-0.111 to 0.430)	0.008 (-0.235 to 0.251)	0.114 (-0.460 to 0.689)	0.096 (-0.106 to 0.298)
Week 17 (N = 17, 15, 15, 47)	0.173 (-0.154 to 0.500)	0.115 (-0.268 to 0.497)	0.083 (-0.610 to 0.776)	0.126 (-0.131 to 0.382)
Week 25 (N = 19, 17, 15, 51)	0.468 (0.182 to 0.754)	0.719 (-0.192 to 1.631)	0.110 (-0.480 to 0.700)	0.446 (0.101 to 0.792)
Week 33 (N = 19, 17, 14, 50)	0.348 (-0.109 to 0.805)	0.417 (-0.241 to 1.076)	0.264 (-0.319 to 0.846)	0.348 (0.044 to 0.651)
Week 41 (N = 17, 16, 13, 46)	0.445 (-0.040 to 0.930)	0.471 (-0.314 to 1.256)	0.845 (-0.091 to 1.782)	0.567 (0.179 to 0.956)
Week 49 (N = 15, 16, 13, 44)	0.360 (-0.117 to 0.837)	0.869 (-0.326 to 2.065)	0.145 (-0.655 to 0.945)	0.482 (-0.007 to 0.970)
Week 57 (N = 16, 16, 11, 43)	1.018 (0.383 to 1.653)	1.573 (-0.263 to 3.408)	0.539 (-0.214 to 1.292)	1.102 (0.399 to 1.804)

Week 65 (N = 18, 15, 12, 45)	1.482 (0.572 to 2.391)	0.988 (0.190 to 1.786)	0.745 (-0.069 to 1.559)	1.121 (0.649 to 1.592)
Week 73 (N = 17, 15, 11, 43)	1.156 (0.242 to 2.071)	1.128 (-0.014 to 2.270)	0.324 (-0.494 to 1.142)	0.933 (0.391 to 1.476)
Week 81 (N = 15, 12, 12, 39)	1.243 (0.311 to 2.174)	0.625 (-0.033 to 1.283)	0.687 (-0.406 to 1.779)	0.882 (0.391 to 1.372)
Week 89 (N = 14, 11, 11, 36)	1.287 (0.332 to 2.242)	0.837 (0.102 to 1.572)	0.460 (-0.469 to 1.389)	0.897 (0.415 to 1.379)
Week 97 (N = 14, 12, 11, 37)	0.928 (0.193 to 1.663)	0.883 (-0.405 to 2.172)	0.670 (-0.393 to 1.733)	0.837 (0.304 to 1.369)
Week 110 (N = 12, 13, 9, 34)	1.085 (0.048 to 2.122)	1.238 (0.382 to 2.095)	0.300 (-0.800 to 1.400)	0.936 (0.410 to 1.462)
Week 122 (N = 8, 10, 7, 25)	1.195 (-0.064 to 2.454)	1.416 (0.650 to 2.182)	0.914 (-0.008 to 1.837)	1.205 (0.719 to 1.690)
Week 146 (N = 4, 4, 5, 13)	2.138 (-0.866 to 5.141)	1.588 (-1.542 to 4.717)	1.662 (0.096 to 3.228)	1.785 (0.840 to 2.731)
Week 170 (N = 1, 2, 1, 4)	3.300 (-99999 to 99999)	2.090 (-99999 to 99999)	1.800 (-99999 to 99999)	2.320 (-1.110 to 5.750)

Notes:

[85] - If no evaluable data collected, 99999 was entered instead.
[86] - If no evaluable data collected, 99999 was entered instead.
[87] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Ankle Range of Motion (ROM) - B5161004 Baseline

End point title	Change From Baseline on the Ankle Range of Motion (ROM) - B5161004 Baseline

End point description:

ROM of the ankle was evaluated by goniometry and any occurrences of ankle contractures were recorded. In order to provide optimal testing conditions and consistency in endpoint measurements, the functional assessment of ankle ROM was completed at approximately the same time of day.
This analysis population included all subjects who had received at least 1 dose of study medication. N=x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13, 25, 49 and 73. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[88]	20[89]	20[90]	59
Units: Degree				
arithmetic mean (confidence interval 95%)				
Left Ankle - Baseline (N=16, 16, 18, 50)	0.6 (-3.7 to 4.8)	-0.4 (-6.8 to 5.9)	-7.8 (-13.8 to -1.9)	-2.8 (-6.0 to 0.4)
Left Ankle - Week 13 (N=16, 16, 17, 49)	-2.1 (-5.2 to 1.0)	-1.0 (-5.2 to 3.2)	-0.9 (-3.7 to 1.8)	-1.3 (-3.2 to 0.5)

Left Ankle - Week 25 (N=11, 12, 14, 37)	-2.2 (-5.4 to 1.0)	-1.8 (-8.7 to 5.0)	-2.4 (-6.4 to 1.5)	-2.2 (-4.7 to 0.4)
Left Ankle - Week 49 (N=7, 6, 7, 20)	-1.7 (-12.0 to 8.6)	-6.2 (-15.2 to 2.9)	-4.0 (-11.4 to 3.4)	-3.9 (-8.1 to 0.4)
Left Ankle - Week 73 (N= 2, 2, 2, 6)	-2.5 (-99999 to 99999)	-3.0 (-99999 to 99999)	0.5 (-99999 to 99999)	-1.7 (-6.8 to 3.4)
Right Ankle - Baseline (N=16, 16, 18, 50)	0.0 (-4.2 to 4.2)	-3.1 (-10.3 to 4.2)	-10.3 (-17.9 to -2.7)	-4.7 (-8.5 to -0.9)
Right Ankle - Week 13 (N=16, 16, 17, 49)	-0.8 (-4.5 to 3.0)	0.4 (-3.0 to 3.9)	0.8 (-2.1 to 3.7)	0.2 (-1.6 to 2.0)
Right Ankle - Week 25 (N=11, 12, 14, 37)	-1.5 (-5.3 to 2.2)	-1.7 (-7.0 to 3.6)	-2.1 (-6.0 to 1.8)	-1.8 (-4.1 to 0.5)
Right Ankle - Week 49 (N= 7, 6, 7, 20)	-4.1 (-12.3 to 4.0)	-3.3 (-6.1 to -0.5)	-3.0 (-6.1 to 0.1)	-3.5 (-6.1 to -0.9)
Right Ankle - Week 73 (N=2, 2, 2, 6)	-1.0 (-99999 to 99999)	3.0 (-99999 to 99999)	5.5 (-99999 to 99999)	2.5 (-7.1 to 12.1)

Notes:

[88] - If no evaluable data collected, 99999 was entered instead.

[89] - If no evaluable data collected, 99999 was entered instead.

[90] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Ankle ROM - Overall Baseline

End point title	Change From Baseline on the Ankle ROM - Overall Baseline

End point description:

ROM of the ankle was evaluated by goniometry and any occurrences of ankle contractures were recorded. In order to provide optimal testing conditions and consistency in endpoint measurements, the functional assessment of ankle ROM was completed at approximately the same time of day. This is the overall change from baseline which included the change since enrolling in the parent study B5161002. This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 9,17,25,33,41,49,57,65,73,81,89,97,110,122,146,170. Overall baseline was defined as the last pre-dose assessment prior to the first day of dosing in study B5161002. Week 1 was counted starting from the study treatment in study B5161002.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[91]	20[92]	20[93]	59
Units: Degree				
arithmetic mean (confidence interval 95%)				
Left Ankle - Baseline (N = 19, 20, 20, 59)	7.1 (4.7 to 9.5)	2.6 (-1.8 to 6.9)	1.6 (-1.3 to 4.4)	3.7 (1.8 to 5.6)
Left Ankle - Week 9 (N = 19, 19, 20, 58)	-1.8 (-4.1 to 0.4)	-0.8 (-3.6 to 2.1)	-0.2 (-2.7 to 2.3)	-0.9 (-2.3 to 0.5)
Left Ankle - Week 17 (N = 19, 20, 20, 59)	-2.5 (-5.5 to 0.4)	-2.0 (-4.4 to 0.4)	-1.0 (-3.4 to 1.4)	-1.8 (-3.2 to -0.4)
Left Ankle - Week 25 (N = 19, 20, 19, 58)	-2.3 (-5.5 to 1.0)	-4.7 (-7.6 to -1.8)	0.0 (-2.0 to 2.0)	-2.4 (-3.9 to -0.8)

Left Ankle - Week 33 (N = 19, 20, 20, 59)	-1.1 (-4.9 to 2.7)	-2.4 (-5.1 to 0.3)	-1.9 (-3.8 to 0.0)	-1.8 (-3.4 to -0.2)
Left Ankle - Week 41 (N = 18, 20, 20, 58)	-2.4 (-6.0 to 1.2)	-3.8 (-6.3 to -1.2)	-2.1 (-4.6 to 0.4)	-2.8 (-4.3 to -1.2)
Left Ankle - Week 49 (N = 19, 20, 20, 59)	-3.2 (-6.6 to 0.2)	-5.5 (-8.9 to -2.1)	-2.3 (-5.4 to 0.9)	-3.7 (-5.5 to -1.8)
Left Ankle - Week 57 (N = 19, 20, 18, 57)	-3.5 (-6.5 to -0.6)	-6.1 (-10.4 to -1.7)	-5.8 (-10.0 to -1.6)	-5.1 (-7.3 to -3.0)
Left Ankle - Week 65 (N = 19, 20, 19, 58)	-4.1 (-7.8 to -0.3)	-5.4 (-12.6 to 1.9)	-5.2 (-9.3 to -1.1)	-4.9 (-7.8 to -2.0)
Left Ankle - Week 73 (N = 19, 20, 20, 59)	-2.5 (-6.6 to 1.6)	-4.6 (-12.2 to 3.1)	-6.6 (-10.4 to -2.7)	-4.6 (-7.6 to -1.5)
Left Ankle - Week 81 (N = 19, 18, 20, 57)	-6.1 (-10.7 to -1.5)	-2.7 (-9.6 to 4.3)	-8.7 (-13.2 to -4.1)	-5.9 (-8.9 to -2.9)
Left Ankle - Week 89 (N = 18, 20, 19, 57)	-9.9 (-16.2 to -3.7)	-6.3 (-16.0 to 3.4)	-8.4 (-13.6 to -3.1)	-8.1 (-12.2 to -4.1)
Left Ankle - Week 97 (N = 19, 20, 20, 59)	-7.9 (-14.1 to -1.8)	-10.0 (-16.7 to -3.2)	-9.3 (-13.7 to -4.8)	-9.1 (-12.2 to -5.9)
Left Ankle - Week 110 (N = 16, 16, 17, 49)	-8.3 (-14.2 to -2.4)	-5.9 (-12.8 to 1.0)	-9.9 (-15.4 to -4.4)	-8.1 (-11.4 to -4.8)
Left Ankle - Week 122 (N = 11, 12, 14, 37)	-8.7 (-16.4 to -1.1)	-5.7 (-12.8 to 1.5)	-11.5 (-19.0 to -4.0)	-8.8 (-12.7 to -4.8)
Left Ankle - Week 146 (N = 7, 6, 7, 20)	-10.0 (-21.7 to 1.7)	-10.8 (-19.7 to -1.9)	-10.9 (-22.9 to 1.2)	-10.6 (-15.7 to -5.4)
Left Ankle - Week 170 (N = 2, 2, 2, 6)	-6.5 (-99999 to 99999)	-6.0 (-99999 to 99999)	-9.0 (-99999 to 99999)	-7.2 (-13.4 to -1.0)
Right Ankle - Baseline (N = 19, 20, 20, 59)	6.7 (4.4 to 9.1)	1.0 (-4.0 to 6.0)	1.5 (-1.6 to 4.6)	3.0 (0.9 to 5.1)
Right Ankle - Week 9 (N = 19, 19, 20, 58)	-1.9 (-5.0 to 1.2)	-0.8 (-3.5 to 1.9)	-1.3 (-3.6 to 1.0)	-1.3 (-2.8 to 0.2)
Right Ankle - Week 17 (N = 19, 20, 20, 59)	-2.2 (-6.3 to 2.0)	-1.8 (-3.9 to 0.3)	-2.0 (-4.8 to 0.9)	-2.0 (-3.7 to -0.3)
Right Ankle - Week 25 (N = 19, 20, 20, 59)	-1.5 (-5.2 to 2.1)	-4.5 (-7.6 to -1.3)	-3.1 (-5.8 to -0.4)	-3.1 (-4.8 to -1.3)
Right Ankle - Week 33 (N = 19, 20, 20, 59)	0.4 (-3.7 to 4.5)	-1.6 (-4.7 to 1.6)	-3.4 (-5.9 to -0.8)	-1.5 (-3.3 to 0.3)
Right Ankle - Week 41 (N = 19, 20, 20, 59)	-2.7 (-6.0 to 0.6)	-3.1 (-6.0 to -0.1)	-2.7 (-5.7 to 0.4)	-2.8 (-4.5 to -1.1)
Right Ankle - Week 49 (N = 19, 20, 20, 59)	-3.8 (-7.6 to -0.1)	-4.5 (-7.9 to -1.1)	-2.5 (-6.3 to 1.4)	-3.6 (-5.6 to -1.6)
Right Ankle - Week 57 (N = 19, 20, 18, 57)	-2.5 (-6.1 to 1.0)	-5.3 (-9.8 to -0.8)	-7.9 (-12.4 to -3.5)	-5.2 (-7.6 to -2.9)
Right Ankle - Week 65 (N = 19, 20, 19, 58)	-4.7 (-9.1 to -0.4)	-5.4 (-12.6 to 1.9)	-6.6 (-10.8 to -2.4)	-5.6 (-8.5 to -2.6)
Right Ankle - Week 73 (N = 19, 20, 20, 59)	-3.6 (-8.0 to 0.8)	-3.0 (-10.1 to 4.2)	-8.0 (-12.6 to -3.4)	-4.9 (-7.9 to -1.8)
Right Ankle - Week 81 (N = 19, 18, 20, 57)	-5.1 (-9.7 to -0.5)	-1.4 (-7.9 to 5.1)	-10.0 (-14.9 to -5.1)	-5.6 (-8.7 to -2.6)
Right Ankle - Week 89 (N = 18, 20, 19, 57)	-9.4 (-15.4 to -3.4)	-6.8 (-15.4 to 1.9)	-10.4 (-15.8 to -5.0)	-8.8 (-12.6 to -5.0)
Right Ankle - Week 97 (N = 19, 20, 20, 59)	-7.5 (-12.4 to -2.5)	-10.6 (-18.3 to -2.9)	-11.8 (-17.5 to -6.1)	-10.0 (-13.4 to -6.6)
Right Ankle - Week 110 (N = 16, 16, 17, 49)	-7.4 (-13.9 to -0.9)	-5.9 (-11.6 to -0.2)	-10.4 (-16.4 to -4.3)	-7.9 (-11.2 to -4.6)
Right Ankle - Week 122 (N = 11, 12, 14, 37)	-7.6 (-14.9 to -0.3)	-6.8 (-14.3 to 0.6)	-12.7 (-20.1 to -5.3)	-9.3 (-13.3 to -5.3)
Right Ankle - Week 146 (N = 7, 6, 7, 20)	-12.6 (-24.4 to -0.7)	-9.2 (-20.6 to 2.2)	-12.1 (-23.5 to -0.7)	-11.4 (-16.8 to -6.0)
Right Ankle - Week 170 (N = 2, 2, 2, 6)	-7.5 (-99999 to 99999)	-3.5 (-99999 to 99999)	-12.0 (-99999 to 99999)	-7.7 (-16.3 to 1.0)

Notes:

[91] - If no evaluable data collected, 99999 was entered instead.

[92] - If no evaluable data collected, 99999 was entered instead.

[93] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Performance of Upper Limb (PUL) Overall Score - B5161004 Baseline

End point title	Change From Baseline on the Performance of Upper Limb (PUL) Overall Score - B5161004 Baseline

End point description:

The PUL scale was used to assess motor performance of the upper limb for individuals with DMD. The PUL scale includes 22 items;an entry item defining the starting functional level, and 21 items subdivided into 3 levels; shoulder(4items), middle(9items) and distal(8items). Scoring options per item may not be uniform and may vary from 0-1 to 0-6, according to the performance, with higher values corresponding to better performance.A total maximum score of 74 is achieved by adding the individual level scores; shoulder maximum 16, middle level maximum score 34 and distal level maximum score 24.In order to provide optimal testing conditions and consistency in endpoint measurements, the functional assessment of PUL was completed at approximately the same time of day.This analysis population included all subjects who had received at least 1 dose of study medication. N=x,y,z,t in the following table represents the number of evaluable subjects in Sequence groups 1,2,3 andTotal.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13, 25, 49 and 73. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[94]	20[95]	20[96]	59
Units: Units on a Scale				
arithmetic mean (confidence interval 95%)				
Baseline (N=15,16,17,48)	65.6 (63.0 to 68.2)	65.3 (61.4 to 69.1)	63.8 (59.9 to 67.8)	64.9 (62.9 to 66.8)
Week 13 (N=14,16,16,46)	-1.2 (-2.3 to -0.1)	-1.5 (-2.6 to -0.4)	-1.8 (-3.7 to 0.0)	-1.5 (-2.3 to -0.8)
Week 25 (N=9,11,13,33)	-1.2 (-2.3 to -0.2)	-3.0 (-5.3 to -0.7)	-0.3 (-1.2 to 0.6)	-1.5 (-2.4 to -0.6)
Week 49 (N=7,6,7,20)	-1.6 (-5.5 to 2.4)	-7.8 (-14.1 to -1.6)	-2.6 (-6.3 to 1.1)	-3.8 (-6.3 to -1.3)
Week 73 (N=2,2,2,6)	-13.5 (-99999 to 99999)	-7.5 (-99999 to 99999)	-6.0 (-99999 to 99999)	-9.0 (-15.0 to -3.0)

Notes:

[94] - If no evaluable data collected, 99999 was entered instead.

[95] - If no evaluable data collected, 99999 was entered instead.

[96] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the PUL Overall Score - Overall Baseline

End point title	Change From Baseline on the PUL Overall Score - Overall Baseline

End point description:

The PUL scale was used to assess motor performance of the upper limb for individuals with DMD. The PUL scale includes 22 items; an entry item defining the starting functional level, and 21 items subdivided into 3 levels; shoulder (4 items),middle (9 items) and distal (8 items). Scoring options per item may not be uniform and may vary from 0 -1 to 0 -6, according to the performance, with higher values corresponding to better performance. Mayhew, A., et al. (2013). "Development of the Performance of the Upper Limb module for Duchenne muscular dystrophy." Dev Med Child Neurol 55(11): 1038-1045. The PUL assessment was completed at approximately the same time of day. This is the overall change from baseline which included the change since enrolling in parent study B5161002. This analysis population included all subjects who had received at least 1 dose of study medication. N=x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1,2,3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 9,17,25,33,41,49,57,65,73,81,89,97,110,122,146,170. Overall baseline was defined as the last pre-dose assessment prior to the first day of dosing in study B5161002. Week 1 was counted starting from the study treatment in study B5161002.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[97]	20[98]	20[99]	59
Units: Units on a Scale				
arithmetic mean (confidence interval 95%)				
Baseline (N = 19, 20, 20, 59)	66.3 (65.0 to 67.6)	66.9 (64.7 to 69.0)	66.9 (65.1 to 68.6)	66.7 (65.7 to 67.6)
Week 9 (N = 19, 19, 20, 58)	-0.7 (-2.0 to 0.5)	0.5 (-0.7 to 1.7)	-0.1 (-1.0 to 0.8)	-0.1 (-0.7 to 0.5)
Week 17 (N = 19, 20, 19, 58)	-0.5 (-2.6 to 1.5)	-0.2 (-1.3 to 0.9)	-0.4 (-3.1 to 2.2)	-0.4 (-1.5 to 0.7)
Week 25 (N = 18, 19, 20, 57)	0.7 (-1.1 to 2.4)	0.3 (-0.6 to 1.1)	0.2 (-1.5 to 1.8)	0.4 (-0.5 to 1.2)
Week 33 (N = 19, 20, 20, 59)	0.5 (-0.8 to 1.9)	-0.5 (-2.4 to 1.4)	-0.5 (-1.7 to 0.7)	-0.2 (-1.0 to 0.7)
Week 41 (N = 18, 20, 20, 58)	-0.1 (-2.1 to 2.0)	-0.4 (-1.9 to 1.2)	-0.4 (-1.9 to 1.2)	-0.3 (-1.2 to 0.7)
Week 49 (N = 19, 20, 20, 59)	0.1 (-1.6 to 1.8)	-0.8 (-2.9 to 1.4)	-0.5 (-1.9 to 0.9)	-0.4 (-1.4 to 0.6)
Week 57 (N = 19, 17, 19, 55)	-0.3 (-2.2 to 1.5)	-0.8 (-2.9 to 1.4)	-4.7 (-12.0 to 2.6)	-2.0 (-4.6 to 0.6)
Week 65 (N = 18, 20, 20, 58)	0.6 (-1.0 to 2.2)	-0.9 (-3.0 to 1.3)	-4.6 (-11.6 to 2.5)	-1.7 (-4.2 to 0.8)
Week 73 (N = 19, 20, 20, 59)	-1.0 (-2.9 to 0.9)	-1.8 (-4.5 to 0.9)	-1.2 (-3.3 to 1.0)	-1.3 (-2.6 to -0.1)
Week 81 (N = 19, 19, 19, 57)	-0.7 (-2.5 to 1.1)	-1.2 (-3.7 to 1.4)	-1.5 (-3.7 to 0.6)	-1.1 (-2.3 to 0.1)
Week 89 (N = 18, 20, 20, 58)	-0.4 (-2.0 to 1.1)	-2.9 (-7.0 to 1.2)	-2.3 (-4.5 to -0.1)	-1.9 (-3.5 to -0.3)
Week 97 (N = 18, 19, 19, 56)	-1.4 (-3.9 to 1.0)	-2.2 (-5.3 to 0.9)	-2.3 (-5.1 to 0.4)	-2.0 (-3.5 to -0.5)
Week 110 (N = 15, 17, 17, 49)	-1.5 (-3.7 to 0.7)	-3.2 (-6.7 to 0.2)	-4.4 (-8.5 to -0.4)	-3.1 (-5.0 to -1.3)
Week 122 (N = 10, 12, 13, 35)	-1.4 (-5.3 to 2.5)	-2.8 (-6.8 to 1.3)	-2.4 (-5.4 to 0.6)	-2.2 (-4.1 to -0.3)

Week 146 (N = 7, 6, 8, 21)	-2.3 (-7.4 to 2.9)	-6.8 (-15.3 to 1.6)	-2.9 (-7.7 to 2.0)	-3.8 (-6.7 to -0.9)
Week 170 (N = 2, 2, 2, 6)	-14.0 (-99999 to 99999)	-4.0 (-99999 to 99999)	-9.0 (-99999 to 99999)	-9.0 (-17.8 to -0.2)

Notes:

[97] - If no evaluable data collected, 99999 was entered instead.

[98] - If no evaluable data collected, 99999 was entered instead.

[99] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Six Minute Walk Distance (6MWD) - B5161004 Baseline

End point title	Change From Baseline on the Six Minute Walk Distance (6MWD) - B5161004 Baseline

End point description:

The 6MWD evaluated ambulation ability by measuring the distance walked in 6 minutes. In order to provide optimal testing conditions and consistency in endpoint measurements, the functional assessment of 6MWD was completed at approximately the same time of day.
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13, 25, 49 and 73. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[100]	20[101]	20[102]	59
Units: Meters				
arithmetic mean (confidence interval 95%)				
Baseline (N = 15, 13, 11, 39)	328.0 (266.5 to 389.5)	386.2 (341.1 to 431.2)	360.4 (305.1 to 415.6)	356.5 (326.3 to 386.8)
Week 13 (N = 15, 13, 11, 39)	-23.6 (-50.0 to 2.8)	-26.1 (-45.6 to -6.5)	-8.4 (-28.6 to 11.9)	-20.1 (-32.5 to -7.7)
Week 25 (N = 10, 10, 8, 28)	-45.5 (-83.4 to -7.6)	-16.1 (-37.4 to 5.2)	-11.3 (-37.6 to 15.1)	-25.2 (-41.3 to -9.1)
Week 49 (N = 6, 5, 6, 17)	-98.0 (-219.5 to 23.5)	-16.8 (-55.2 to 21.6)	-39.0 (-68.2 to -9.8)	-53.3 (-92.8 to -13.8)
Week 73 (N = 2, 2, 1, 5)	-110.0 (-99999 to 99999)	-41.5 (-99999 to 99999)	-22.0 (-99999 to 99999)	-65.0 (-124.4 to -5.6)

Notes:

[100] - If no evaluable data collected, 99999 was entered instead.

[101] - If no evaluable data collected, 99999 was entered instead.

[102] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the 6MWD - Overall Baseline

End point title	Change From Baseline on the 6MWD - Overall Baseline

End point description:

The 6MWD evaluated ambulation ability by measuring the distance walked in 6 minutes. In order to provide optimal testing conditions and consistency in endpoint measurements, the functional assessment of 6MWD was completed at approximately the same time of day. This is the overall change from baseline which included the change since enrolling in the parent study B5161002.
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline,Weeks 9,17,25,33,41,49,57,65,73,81,89,97,110,122,146,170. Overall baseline was defined as the last pre-dose assessment prior to the first day of dosing in study B5161002. Week 1 was start of the study treatment in parent study B5161002.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[103]	20[104]	20[105]	59
Units: Meters				
arithmetic mean (confidence interval 95%)				
Baseline (N = 19, 20, 20, 59)	409.1 (367.2 to 450.9)	349.4 (290.3 to 408.5)	363.7 (326.0 to 401.4)	373.5 (347.0 to 399.9)
Week 9 (N = 18, 17, 19, 54)	-11.6 (-29.5 to 6.3)	-2.0 (-22.8 to 18.8)	-9.3 (-21.3 to 2.7)	-7.8 (-17.0 to 1.4)
Week 17 (N = 19, 17, 18, 54)	-36.8 (-63.9 to -9.7)	-16.1 (-39.2 to 7.1)	-15.6 (-34.8 to 3.6)	-23.2 (-36.2 to -10.2)
Week 25 (N = 17, 18, 17, 52)	-41.8 (-80.7 to -2.9)	-8.2 (-35.7 to 19.3)	-29.6 (-54.9 to -4.4)	-26.2 (-43.3 to -9.1)
Week 33 (N = 19, 18, 17, 54)	-43.8 (-74.2 to -13.5)	-17.5 (-45.8 to 10.8)	-34.9 (-62.3 to -7.5)	-32.3 (-48.1 to -16.4)
Week 41 (N = 17, 18, 15, 50)	-54.2 (-91.3 to -17.1)	-37.4 (-70.8 to -4.1)	-34.9 (-64.2 to -5.7)	-42.4 (-60.6 to -24.1)
Week 49 (N = 18, 17, 15, 50)	-59.8 (-96.8 to -22.9)	-29.1 (-64.2 to 6.0)	-37.3 (-65.9 to -8.8)	-42.6 (-61.4 to -23.8)
Week 57 (N = 18, 16, 13, 47)	-72.2 (-109.9 to -34.4)	-32.8 (-69.8 to 4.1)	-52.6 (-86.8 to -18.4)	-53.4 (-73.7 to -33.0)
Week 65 (N = 17, 15, 13, 45)	-74.5 (-128.9 to -20.0)	-33.3 (-71.1 to 4.5)	-58.2 (-106.3 to -10.0)	-56.0 (-82.2 to -29.8)
Week 73 (N = 17, 15, 15, 47)	-77.2 (-119.8 to -34.7)	-35.5 (-70.6 to -0.4)	-60.1 (-102.5 to -17.6)	-58.4 (-80.6 to -36.3)
Week 81 (N = 17, 14, 14, 45)	-78.9 (-120.5 to -37.3)	-42.6 (-94.7 to 9.5)	-39.6 (-64.4 to -14.7)	-55.4 (-78.0 to -32.7)
Week 89 (N = 16, 13, 12, 41)	-96.7 (-141.5 to -51.9)	-33.7 (-73.3 to 5.9)	-41.5 (-63.8 to -19.2)	-60.6 (-83.2 to -37.9)
Week 97 (N = 17, 13, 13, 43)	-80.7 (-131.4 to -30.1)	-25.1 (-64.0 to 13.9)	-55.3 (-79.3 to -31.3)	-56.2 (-79.8 to -32.6)
Week 110 (N = 16, 17, 16, 49)	-115.5 (-171.8 to -59.2)	-87.9 (-141.6 to -34.1)	-126.1 (-189.2 to -63.0)	-109.4 (-140.6 to -78.2)
Week 122 (N = 11, 12, 13, 36)	-142.5 (-229.0 to -56.1)	-69.8 (-144.7 to 5.0)	-155.0 (-231.0 to -79.0)	-122.8 (-165.6 to -80.0)
Week 146 (N = 6, 6, 7, 19)	-224.0 (-454.5 to 6.5)	-53.2 (-179.5 to 73.2)	-137.1 (-209.0 to -65.3)	-138.1 (-213.2 to -62.9)
Week 170 (N = 2, 2, 2, 6)	-184.0 (-99999 to 99999)	-90.5 (-99999 to 99999)	-206.5 (-99999 to 99999)	-160.3 (-294.3 to -26.4)

Notes:

[103] - If no evaluable data collected, 99999 was entered instead.

[104] - If no evaluable data collected, 99999 was entered instead.

[105] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on the Forced Expiratory Volume in one second (FEV1) - B5161004 Baseline

End point title	Change from Baseline on the Forced Expiratory Volume in one second (FEV1) - B5161004 Baseline

End point description:

The FEV1 was recorded as an absolute volume in litres and in terms of predicted values according to age, height, race and gender. The best single FEV1 measurement from a set of 3 was recorded in the database.
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13, 25, 49 and 73. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[106]	20[107]	20[108]	59
Units: Litre				
arithmetic mean (confidence interval 95%)				
FEV1 - Baseline (N = 16, 17, 17, 50)	1.3694 (1.1372 to 1.6015)	1.4235 (1.1693 to 1.6777)	1.5335 (1.3687 to 1.6983)	1.4436 (1.3243 to 1.5629)
FEV1 - Week 13 (N = 16, 15, 14, 45)	0.1113 (-0.0094 to 0.2319)	0.1307 (-0.0040 to 0.2653)	-0.0014 (-0.1178 to 0.1150)	0.0827 (0.0144 to 0.1509)
FEV1 - Week 25 (N = 11, 12, 13, 36)	0.1473 (-0.0405 to 0.3351)	0.1175 (0.0093 to 0.2257)	0.0923 (-0.0524 to 0.2370)	0.1175 (0.0406 to 0.1944)
FEV1 - Week 49 (N = 7, 6, 6, 19)	0.3057 (0.0016 to 0.6098)	0.2083 (-0.0561 to 0.4728)	0.1000 (-0.0167 to 0.2167)	0.2100 (0.0874 to 0.3326)
FEV1 - Week 73 (N = 2, 2, 1, 5)	0.7500 (-99999 to 99999)	0.2550 (-99999 to 99999)	0.2800 (-99999 to 99999)	0.4580 (-0.3052 to 1.2212)

Notes:

[106] - If no evaluable data collected, 99999 was entered instead.

[107] - If no evaluable data collected, 99999 was entered instead.

[108] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on the Peak Expiratory Flow Rate (PEFR)- B5161004 Baseline

End point title	Change from Baseline on the Peak Expiratory Flow Rate (PEFR)- B5161004 Baseline

End point description:

PEFR was one of the Pulmonary Function Tests (PFTs). Three technically adequate peak expiratory flow rate (PEFR) maneuvers were performed and reported in L/min, and the highest single PEFR was reported in the database. In order to provide optimal testing conditions and consistency in endpoint measurements, the functional assessment of PEFR was completed at approximately the same time of day.
This analysis population included all subjects who had received at least 1 dose of study medication. N = x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13, 25, 49 and 73. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[109]	20[110]	20[111]	59
Units: Litres / Minute				
arithmetic mean (confidence interval 95%)				
Baseline (N = 14, 17, 17, 48)	200.314 (154.281 to 246.348)	187.200 (150.135 to 224.265)	185.882 (163.694 to 208.071)	190.558 (171.737 to 209.380)
Week 13 (N = 14, 15, 14, 43)	-17.014 (-56.536 to 22.507)	20.613 (-8.846 to 50.073)	8.214 (-29.197 to 45.626)	4.326 (-15.003 to 23.654)
Week 25 (N = 10, 12, 12, 34)	-16.260 (-59.079 to 26.559)	0.767 (-22.311 to 23.845)	39.250 (6.034 to 72.466)	9.341 (-9.379 to 28.061)
Week 49 (N = 7, 6, 6, 19)	-31.171 (-94.943 to 32.600)	11.700 (-55.267 to 78.667)	50.967 (-1.595 to 103.529)	8.305 (-24.489 to 41.099)
Week 73 (N = 2, 2, 1, 5)	6.800 (-99999 to 99999)	5.600 (-99999 to 99999)	36.000 (-99999 to 99999)	12.160 (-81.893 to 106.213)

Notes:

[109] - If no evaluable data collected, 99999 was entered instead.

[110] - If no evaluable data collected, 99999 was entered instead.

[111] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Myometry Based Muscle Strength - B5161004 Baseline

End point title	Change From Baseline on the Myometry Based Muscle Strength - B5161004 Baseline

End point description:

Muscle strength was quantified by means of a handheld dynamometer. The following muscle groups were evaluated: knee extension, elbow flexion, elbow extension, hip abduction and shoulder abduction. 95% Confidence Interval was not calculated when less than or equal to 3 subjects' data were available. This analysis population included all subjects who had received at least 1 dose of study medication. Not all subjects had evaluable data at each category.

End point type	Secondary

End point timeframe:

Baseline, Weeks 13, 25, 49, 73. Baseline was defined as the last assessment prior to dosing on Day 1 in B5161004. Week 1 was counted starting from the study treatment in study B5161004.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[112]	20[113]	20[114]	59
Units: Kilograms				
arithmetic mean (confidence interval 95%)				
Elbow Extension-Left - Baseline	3.35 (2.47 to 4.23)	3.24 (2.58 to 3.89)	2.83 (2.13 to 3.52)	3.13 (2.72 to 3.53)
Elbow Extension-Left - Week 13	-0.21 (-0.55 to 0.14)	-0.55 (-1.11 to 0.01)	-0.31 (-0.81 to 0.18)	-0.36 (-0.62 to -0.10)
Elbow Extension-Left - Week 25	-0.44 (-0.94 to 0.07)	-0.38 (-1.13 to 0.36)	-0.09 (-0.63 to 0.45)	-0.29 (-0.61 to 0.03)
Elbow Extension-Left - Week 49	-0.66 (-1.93 to 0.61)	-0.47 (-1.05 to 0.12)	-0.23 (-0.67 to 0.22)	-0.45 (-0.86 to -0.04)
Elbow Extension-Left - Week 73	-1.15 (-99999 to 99999)	-0.95 (-99999 to 99999)	-0.10 (-99999 to 99999)	-0.73 (-1.46 to 0.00)
Elbow Extension-Right - Baseline	3.31 (2.36 to 4.26)	3.24 (2.53 to 3.95)	2.94 (2.29 to 3.60)	3.16 (2.74 to 3.57)
Elbow Extension-Right - Week 13	-0.23 (-0.61 to 0.15)	-0.42 (-1.05 to 0.21)	-0.27 (-0.71 to 0.17)	-0.31 (-0.58 to -0.04)
Elbow Extension-Right - Week 25	-0.40 (-1.05 to 0.25)	-0.68 (-1.21 to -0.14)	0.06 (-0.41 to 0.53)	-0.31 (-0.61 to -0.01)
Elbow Extension-Right - Week 49	-0.59 (-1.82 to 0.65)	-0.60 (-1.07 to -0.13)	-0.07 (-0.55 to 0.41)	-0.41 (-0.82 to 0.00)
Elbow Extension-Right - Week 73	-0.70 (-99999 to 99999)	-1.25 (-99999 to 99999)	0.20 (-99999 to 99999)	-0.58 (-1.35 to 0.18)
Elbow Flexion-Left - Baseline	4.14 (2.79 to 5.49)	3.74 (3.01 to 4.46)	3.19 (2.50 to 3.88)	3.67 (3.15 to 4.19)
Elbow Flexion-Left - Week 13	-0.49 (-1.15 to 0.17)	-0.22 (-0.92 to 0.49)	-0.36 (-0.85 to 0.12)	-0.35 (-0.69 to -0.02)
Elbow Flexion-Left - Week 25	-0.65 (-1.50 to 0.21)	-0.58 (-1.69 to 0.52)	-0.19 (-0.54 to 0.15)	-0.45 (-0.87 to -0.04)
Elbow Flexion-Left - Week 49	-1.13 (-2.97 to 0.71)	-0.08 (-1.33 to 1.16)	-0.39 (-1.10 to 0.33)	-0.56 (-1.22 to 0.11)
Elbow Flexion-Left - Week 73	-1.25 (-99999 to 99999)	-1.55 (-99999 to 99999)	-0.05 (-99999 to 99999)	-0.95 (-2.09 to 0.19)
Elbow Flexion - Right - Baseline	4.13 (2.85 to 5.40)	4.18 (3.33 to 5.02)	3.07 (2.45 to 3.69)	3.77 (3.25 to 4.28)
Elbow Flexion - Right - Week 13	-0.48 (-1.15 to 0.20)	-0.85 (-1.53 to -0.17)	-0.18 (-0.50 to 0.14)	-0.50 (-0.82 to -0.18)
Elbow Flexion - Right - Week 25	-0.75 (-2.03 to 0.53)	-1.08 (-2.04 to -0.11)	0.32 (-0.03 to 0.67)	-0.44 (-0.93 to 0.05)
Elbow Flexion - Right - Week 49	-0.49 (-1.89 to 0.92)	-1.27 (-2.25 to -0.29)	-0.36 (-0.62 to -0.10)	-0.68 (-1.18 to -0.17)
Elbow Flexion - Right - Week 73	-1.25 (-99999 to 99999)	-1.20 (-99999 to 99999)	-0.70 (-99999 to 99999)	-1.05 (-1.46 to -0.64)

Hip Abduction - Left - Baseline	4.23 (2.91 to 5.54)	5.29 (4.32 to 6.25)	4.92 (4.28 to 5.57)	4.82 (4.28 to 5.37)
Hip Abduction - Left - Week 13	0.06 (-0.40 to 0.51)	-0.46 (-1.43 to 0.50)	-0.26 (-1.19 to 0.67)	-0.23 (-0.67 to 0.22)
Hip Abduction - Left - Week 25	-0.08 (-1.38 to 1.22)	-0.75 (-1.63 to 0.13)	-0.11 (-0.78 to 0.56)	-0.32 (-0.81 to 0.17)
Hip Abduction - Left - Week 49	-0.81 (-3.04 to 1.41)	-0.94 (-1.98 to 0.10)	0.00 (-0.72 to 0.72)	-0.55 (-1.30 to 0.21)
Hip Abduction - Left - Week 73	-0.75 (-99999 to 99999)	-2.20 (-99999 to 99999)	0.30 (-99999 to 99999)	-1.12 (-2.83 to 0.59)
Hip Abduction - Right - Baseline	4.39 (2.80 to 5.98)	5.55 (4.44 to 6.67)	4.99 (4.23 to 5.75)	4.99 (4.34 to 5.64)
Hip Abduction - Right - Week 13	-0.04 (-0.59 to 0.52)	-0.75 (-1.94 to 0.43)	-0.51 (-1.42 to 0.41)	-0.44 (-0.95 to 0.07)
Hip Abduction - Right - Week 25	-0.10 (-1.77 to 1.57)	-0.94 (-2.44 to 0.56)	-0.52 (-1.54 to 0.51)	-0.54 (-1.26 to 0.18)
Hip Abduction - Right - Week 49	-1.10 (-3.88 to 1.68)	-0.66 (-2.74 to 1.42)	0.01 (-1.33 to 1.36)	-0.57 (-1.61 to 0.46)
Hip Abduction - Right - Week 73	-0.30 (-99999 to 99999)	-2.15 (-99999 to 99999)	0.30 (-99999 to 99999)	-0.92 (-3.05 to 1.21)
Knee Extension - Left - Baseline	4.21 (3.01 to 5.40)	4.54 (3.40 to 5.68)	4.59 (3.10 to 6.08)	4.45 (3.76 to 5.15)
Knee Extension - Left - Week 13	-0.34 (-0.99 to 0.30)	-0.44 (-1.28 to 0.40)	-1.02 (-1.85 to -0.19)	-0.61 (-1.04 to -0.18)
Knee Extension - Left - Week 25	-0.60 (-1.37 to 0.17)	-0.73 (-1.85 to 0.38)	-0.92 (-1.66 to -0.18)	-0.76 (-1.23 to -0.30)
Knee Extension - Left - Week 49	-0.34 (-1.15 to 0.46)	-0.07 (-0.88 to 0.74)	-0.54 (-1.51 to 0.43)	-0.33 (-0.74 to 0.08)
Knee Extension - Left - Week 73	-0.60 (-99999 to 99999)	0.00 (-99999 to 99999)	-0.25 (-99999 to 99999)	-0.28 (-0.76 to 0.19)
Knee Extension - Right - Baseline	4.33 (3.09 to 5.58)	4.48 (3.53 to 5.44)	4.81 (3.16 to 6.46)	4.55 (3.83 to 5.27)
Knee Extension - Right - Week 13	-0.35 (-1.26 to 0.56)	-0.13 (-0.89 to 0.63)	-0.93 (-1.82 to -0.03)	-0.47 (-0.94 to 0.00)
Knee Extension - Right - Week 25	-0.35 (-1.10 to 0.39)	-1.08 (-1.80 to -0.36)	-0.94 (-1.71 to -0.16)	-0.81 (-1.22 to -0.41)
Knee Extension - Right - Week 49	-0.74 (-1.71 to 0.22)	-0.23 (-1.64 to 1.18)	-0.69 (-2.33 to 0.96)	-0.57 (-1.21 to 0.07)
Knee Extension - Right - Week 73	-0.45 (-99999 to 99999)	-1.35 (-99999 to 99999)	-0.45 (-99999 to 99999)	-0.75 (-1.72 to 0.22)
Shoulder Abduction - Left - Baseline	3.83 (2.83 to 4.83)	3.95 (3.37 to 4.52)	3.75 (3.08 to 4.42)	3.84 (3.44 to 4.25)
Shoulder Abduction - Left - Week 13	-0.14 (-0.71 to 0.43)	-0.31 (-0.95 to 0.34)	-0.28 (-0.69 to 0.14)	-0.24 (-0.54 to 0.05)
Shoulder Abduction - Left - Week 25	-0.29 (-1.22 to 0.64)	-0.53 (-1.21 to 0.16)	-0.44 (-0.81 to -0.06)	-0.42 (-0.76 to -0.08)
Shoulder Abduction - Left - Week 49	-0.44 (-2.36 to 1.47)	-0.45 (-1.88 to 0.98)	-0.50 (-0.77 to -0.23)	-0.47 (-1.10 to 0.17)
Shoulder Abduction - Left - Week 73	-0.75 (-99999 to 99999)	-1.30 (-99999 to 99999)	0.20 (-99999 to 99999)	-0.62 (-1.84 to 0.61)
Shoulder Abduction - Right - Baseline	3.99 (2.72 to 5.26)	4.26 (3.29 to 5.23)	3.91 (3.10 to 4.71)	4.05 (3.51 to 4.60)
Shoulder Abduction - Right - Week 13	-0.16 (-0.75 to 0.44)	-0.55 (-1.50 to 0.40)	-0.39 (-0.96 to 0.18)	-0.37 (-0.76 to 0.02)
Shoulder Abduction - Right - Week 25	-0.05 (-1.02 to 0.91)	-0.81 (-1.89 to 0.27)	-0.59 (-1.34 to 0.16)	-0.50 (-0.99 to -0.01)
Shoulder Abduction - Right - Week 49	-0.49 (-2.95 to 1.98)	-0.60 (-1.78 to 0.58)	-0.16 (-0.58 to 0.27)	-0.41 (-1.17 to 0.36)
Shoulder Abduction - Right - Week 73	-0.30 (-99999 to 99999)	-1.55 (-99999 to 99999)	-0.60 (-99999 to 99999)	-0.82 (-1.51 to -0.12)

Notes:

[112] - If no evaluable data collected, 99999 was entered instead.

[113] - If no evaluable data collected, 99999 was entered instead.

[114] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Myometry Based Muscle Strength - Overall Baseline

End point title	Change From Baseline on the Myometry Based Muscle Strength - Overall Baseline

End point description:

Muscle strength was quantified by means of a handheld dynamometer. The following muscle groups were evaluated: knee extension, elbow flexion, elbow extension, hip abduction and shoulder abduction. 95% Confidence Interval was not calculated when less than or equal to 3 subjects' data were available. This analysis population included all subjects who had received at least 1 dose of study medication. Not all subjects had evaluable data at each category.

End point type	Secondary

End point timeframe:

Baseline,Weeks 9,17,25,33,41,49,57,65,73,81,89,97,110,122,146,170. Overall baseline was defined as the last pre-dose assessment prior to the first day of dosing in study B5161002. Week 1 was start of the study treatment in parent study B5161002.

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19[115]	20[116]	20[117]	59
Units: Kilograms				
arithmetic mean (confidence interval 95%)				
Elbow Extension-Left - Baseline	3.76 (2.48 to 5.05)	3.51 (2.46 to 4.55)	2.90 (2.25 to 3.55)	3.38 (2.82 to 3.94)
Elbow Extension-Left - Week 9	-0.10 (-0.67 to 0.47)	0.76 (-0.09 to 1.61)	0.20 (-0.09 to 0.48)	0.29 (-0.05 to 0.63)
Elbow Extension-Left - Week 17	0.08 (-0.60 to 0.77)	-0.15 (-1.04 to 0.74)	0.17 (-0.17 to 0.50)	0.04 (-0.33 to 0.40)
Elbow Extension-Left - Week 25	-0.74 (-1.75 to 0.26)	-0.03 (-1.07 to 1.01)	-0.02 (-0.30 to 0.26)	-0.25 (-0.71 to 0.21)
Elbow Extension-Left - Week 33	-0.65 (-1.56 to 0.26)	-0.37 (-1.08 to 0.34)	0.19 (-0.23 to 0.62)	-0.28 (-0.67 to 0.12)
Elbow Extension-Left - Week 41	-0.43 (-1.82 to 0.96)	-0.20 (-1.04 to 0.64)	-0.02 (-0.36 to 0.33)	-0.22 (-0.73 to 0.30)
Elbow Extension-Left - Week 49	-0.65 (-1.76 to 0.45)	-0.46 (-1.30 to 0.37)	0.25 (-0.14 to 0.65)	-0.29 (-0.75 to 0.17)
Elbow Extension-Left - Week 57	-0.75 (-1.77 to 0.26)	-0.60 (-1.41 to 0.21)	-0.01 (-0.31 to 0.30)	-0.46 (-0.90 to -0.03)
Elbow Extension-Left - Week 65	-0.70 (-1.62 to 0.22)	-0.30 (-1.36 to 0.76)	0.12 (-0.25 to 0.48)	-0.29 (-0.76 to 0.17)
Elbow Extension-Left - Week 73	-0.87 (-1.85 to 0.10)	-0.19 (-1.11 to 0.73)	0.27 (-0.16 to 0.70)	-0.24 (-0.69 to 0.21)
Elbow Extension-Left - Week 81	-0.75 (-1.65 to 0.15)	-0.44 (-1.21 to 0.33)	0.22 (-0.17 to 0.61)	-0.31 (-0.70 to 0.09)

Elbow Extension-Left - Week 89	-0.63 (-1.54 to 0.29)	-0.69 (-1.39 to 0.02)	0.09 (-0.36 to 0.54)	-0.40 (-0.79 to -0.01)
Elbow Extension-Left - Week 97	-0.69 (-1.66 to 0.28)	-0.49 (-1.22 to 0.24)	-0.05 (-0.47 to 0.38)	-0.40 (-0.81 to 0.00)
Elbow Extension-Left - Week 110	-0.99 (-2.00 to 0.01)	-1.08 (-2.21 to 0.05)	-0.36 (-0.84 to 0.12)	-0.81 (-1.31 to -0.31)
Elbow Extension-Left - Week 122	-1.81 (-3.30 to -0.32)	-0.58 (-1.56 to 0.40)	0.06 (-0.26 to 0.38)	-0.71 (-1.26 to -0.15)
Elbow Extension-Left - Week 146	-1.90 (-4.56 to 0.76)	-0.72 (-2.15 to 0.72)	0.06 (-0.43 to 0.54)	-0.86 (-1.79 to 0.07)
Elbow Extension-Left - Week 170	-4.55 (-99999 to 99999)	-0.20 (-99999 to 99999)	-0.20 (-99999 to 99999)	-1.65 (-4.05 to 0.75)
Elbow Extension-Right - Baseline	3.85 (2.63 to 5.06)	3.49 (2.31 to 4.67)	2.96 (2.25 to 3.66)	3.42 (2.85 to 4.00)
Elbow Extension-Right - Week 9	-0.43 (-1.11 to 0.25)	0.77 (-0.28 to 1.82)	0.26 (-0.02 to 0.53)	0.20 (-0.22 to 0.62)
Elbow Extension-Right - Week 17	0.03 (-0.88 to 0.93)	0.08 (-1.02 to 1.19)	0.30 (0.00 to 0.59)	0.14 (-0.31 to 0.59)
Elbow Extension-Right - Week 25	-0.64 (-1.54 to 0.27)	0.13 (-0.91 to 1.16)	0.27 (0.03 to 0.51)	-0.07 (-0.52 to 0.38)
Elbow Extension-Right - Week 33	-0.74 (-1.77 to 0.29)	-0.39 (-1.22 to 0.45)	0.20 (-0.18 to 0.58)	-0.30 (-0.74 to 0.14)
Elbow Extension-Right - Week 41	-0.61 (-1.74 to 0.52)	-0.44 (-1.22 to 0.35)	-0.12 (-0.47 to 0.24)	-0.39 (-0.84 to 0.06)
Elbow Extension-Right - Week 49	-0.56 (-1.68 to 0.56)	-0.45 (-1.27 to 0.38)	0.04 (-0.25 to 0.33)	-0.32 (-0.77 to 0.13)
Elbow Extension-Right - Week 57	-1.01 (-1.98 to -0.04)	-0.65 (-1.50 to 0.21)	0.09 (-0.18 to 0.36)	-0.53 (-0.96 to -0.09)
Elbow Extension-Right - Week 65	-0.88 (-1.85 to 0.09)	-0.20 (-1.34 to 0.94)	0.28 (-0.14 to 0.71)	-0.26 (-0.77 to 0.24)
Elbow Extension-Right - Week 73	-1.07 (-2.08 to -0.07)	-0.26 (-1.36 to 0.85)	0.17 (-0.23 to 0.57)	-0.37 (-0.88 to 0.13)
Elbow Extension-Right - Week 81	-0.71 (-1.68 to 0.27)	-0.67 (-1.61 to 0.26)	0.59 (0.18 to 0.99)	-0.25 (-0.71 to 0.21)
Elbow Extension-Right - Week 89	-1.00 (-2.08 to 0.08)	-0.58 (-1.40 to 0.24)	0.17 (-0.23 to 0.57)	-0.45 (-0.90 to -0.01)
Elbow Extension-Right - Week 97	-0.76 (-1.76 to 0.24)	-0.48 (-1.50 to 0.54)	-0.04 (-0.38 to 0.31)	-0.42 (-0.88 to 0.04)
Elbow Extension-Right - Week 110	-1.12 (-2.21 to -0.03)	-0.94 (-2.10 to 0.23)	-0.38 (-0.92 to 0.17)	-0.80 (-1.33 to -0.28)
Elbow Extension-Right - Week 122	-1.77 (-3.53 to -0.01)	-0.63 (-1.25 to -0.02)	0.14 (-0.34 to 0.61)	-0.65 (-1.21 to -0.09)
Elbow Extension-Right - Week 146	-1.70 (-4.42 to 1.02)	-0.75 (-1.06 to -0.44)	-0.03 (-0.74 to 0.68)	-0.83 (-1.70 to 0.04)
Elbow Extension-Right - Week 170	-4.35 (-99999 to 99999)	-1.45 (-99999 to 99999)	-0.15 (-99999 to 99999)	-1.98 (-4.01 to 0.04)
Elbow Flexion-Left - Baseline	4.58 (2.96 to 6.19)	4.21 (3.14 to 5.27)	3.83 (3.01 to 4.64)	4.20 (3.54 to 4.85)
Elbow Flexion-Left - Week 9	-0.11 (-1.17 to 0.95)	1.06 (-0.01 to 2.14)	0.01 (-0.46 to 0.47)	0.32 (-0.18 to 0.82)
Elbow Flexion-Left -Week 17	-0.37 (-1.69 to 0.95)	-0.05 (-0.82 to 0.72)	-0.05 (-0.56 to 0.47)	-0.15 (-0.65 to 0.35)
Elbow Flexion-Left - Week 25	-0.72 (-2.29 to 0.85)	0.02 (-1.05 to 1.09)	-0.06 (-0.48 to 0.37)	-0.24 (-0.83 to 0.36)
Elbow Flexion-Left - Week 33	-0.59 (-1.97 to 0.79)	-0.45 (-1.10 to 0.20)	-0.04 (-0.41 to 0.34)	-0.36 (-0.85 to 0.13)
Elbow Flexion-Left - Week 41	-0.77 (-2.40 to 0.87)	-0.41 (-1.11 to 0.29)	-0.34 (-0.75 to 0.06)	-0.50 (-1.06 to 0.06)
Elbow Flexion-Left - Week 49	-1.12 (-2.41 to 0.18)	-0.66 (-1.36 to 0.04)	-0.18 (-0.76 to 0.40)	-0.65 (-1.16 to -0.15)
Elbow Flexion-Left - Week 57	-1.02 (-2.43 to 0.39)	-0.57 (-1.27 to 0.14)	-0.29 (-0.75 to 0.16)	-0.63 (-1.15 to -0.11)

Elbow Flexion-Left - Week 65	-1.01 (-2.39 to 0.38)	-0.67 (-1.52 to 0.18)	-0.20 (-0.60 to 0.20)	-0.63 (-1.15 to -0.10)
Elbow Flexion-Left - Week 73	-1.10 (-2.44 to 0.24)	-0.36 (-1.22 to 0.51)	-0.24 (-0.95 to 0.47)	-0.55 (-1.08 to -0.01)
Elbow Flexion-Left - Week 81	-0.91 (-2.28 to 0.46)	-0.62 (-1.37 to 0.13)	-0.19 (-0.65 to 0.28)	-0.56 (-1.06 to -0.06)
Elbow Flexion-Left - Week 89	-0.84 (-2.19 to 0.51)	-0.84 (-1.58 to -0.11)	-0.35 (-0.85 to 0.15)	-0.67 (-1.14 to -0.19)
Elbow Flexion-Left - Week 97	-0.71 (-2.24 to 0.82)	-0.68 (-1.56 to 0.20)	-0.55 (-1.20 to 0.11)	-0.64 (-1.22 to -0.06)
Elbow Flexion-Left - Week 110	-1.28 (-2.94 to 0.38)	-1.01 (-2.13 to 0.11)	-1.05 (-1.77 to -0.34)	-1.11 (-1.76 to -0.47)
Elbow Flexion-Left - Week 122	-2.32 (-4.57 to -0.06)	-0.95 (-2.06 to 0.16)	-0.61 (-1.13 to -0.08)	-1.23 (-1.97 to -0.49)
Elbow Flexion-Left - Week 146	-1.94 (-4.63 to 0.75)	-0.42 (-2.43 to 1.60)	-0.53 (-1.46 to 0.41)	-0.99 (-1.98 to 0.00)
Elbow Flexion-Left - Week 170	-4.70 (-99999 to 99999)	-1.25 (-99999 to 99999)	-1.25 (-99999 to 99999)	-2.40 (-4.30 to -0.50)
Elbow Flexion-Right - Baseline	4.66 (3.43 to 5.89)	4.24 (3.18 to 5.30)	3.73 (2.93 to 4.53)	4.20 (3.63 to 4.77)
Elbow Flexion-Right - Week 9	-0.47 (-1.39 to 0.45)	0.65 (-0.19 to 1.48)	0.49 (-0.02 to 1.00)	0.23 (-0.21 to 0.66)
Elbow Flexion-Right - Week 17	0.09 (-0.83 to 1.02)	-0.08 (-0.97 to 0.80)	0.11 (-0.23 to 0.45)	0.04 (-0.37 to 0.45)
Elbow Flexion-Right - Week 25	-0.67 (-1.58 to 0.24)	-0.14 (-1.20 to 0.92)	0.00 (-0.44 to 0.44)	-0.26 (-0.73 to 0.20)
Elbow Flexion-Right - Week 33	-0.56 (-1.57 to 0.46)	-0.36 (-1.00 to 0.29)	0.06 (-0.40 to 0.52)	-0.28 (-0.68 to 0.12)
Elbow Flexion-Right - Week 41	-0.60 (-1.90 to 0.70)	-0.29 (-0.95 to 0.38)	-0.26 (-0.70 to 0.18)	-0.38 (-0.85 to 0.09)
Elbow Flexion-Right - Week 49	-0.73 (-1.74 to 0.28)	-0.66 (-1.24 to -0.07)	-0.01 (-0.48 to 0.47)	-0.47 (-0.87 to -0.07)
Elbow Flexion-Right - Week 57	-1.11 (-2.15 to -0.07)	-0.42 (-0.97 to 0.13)	-0.23 (-0.65 to 0.19)	-0.58 (-0.98 to -0.18)
Elbow Flexion-Right - Week 65	-0.77 (-1.72 to 0.18)	-0.33 (-1.09 to 0.43)	-0.06 (-0.50 to 0.37)	-0.39 (-0.80 to 0.02)
Elbow Flexion-Right - Week 73	-0.93 (-1.80 to -0.06)	-0.31 (-1.03 to 0.41)	-0.11 (-0.68 to 0.46)	-0.44 (-0.85 to -0.04)
Elbow Flexion-Right - Week 81	-0.99 (-1.87 to -0.12)	-0.30 (-0.96 to 0.36)	0.03 (-0.48 to 0.53)	-0.42 (-0.81 to -0.02)
Elbow Flexion-Right - Week 89	-0.87 (-1.77 to 0.04)	-0.58 (-1.18 to 0.02)	-0.17 (-0.59 to 0.25)	-0.53 (-0.90 to -0.17)
Elbow Flexion-Right - Week 97	-0.86 (-1.93 to 0.20)	-0.35 (-1.13 to 0.44)	-0.57 (-1.19 to 0.06)	-0.59 (-1.04 to -0.13)
Elbow Flexion-Right - Week 110	-1.30 (-2.44 to -0.16)	-1.22 (-2.29 to -0.16)	-0.85 (-1.46 to -0.25)	-1.12 (-1.64 to -0.61)
Elbow Flexion-Right - Week 122	-2.34 (-4.28 to -0.40)	-0.91 (-2.08 to 0.27)	-0.06 (-0.65 to 0.52)	-0.98 (-1.67 to -0.28)
Elbow Flexion-Right - Week 146	-2.00 (-4.72 to 0.72)	-0.90 (-2.00 to 0.20)	-0.63 (-1.26 to 0.00)	-1.19 (-2.07 to -0.31)
Elbow Flexion-Right - Week 170	-5.35 (-99999 to 99999)	-1.20 (-99999 to 99999)	-1.15 (-99999 to 99999)	-2.57 (-4.87 to -0.26)
Hip Abduction-Left - Baseline	4.31 (3.23 to 5.38)	5.10 (3.84 to 6.36)	4.35 (3.56 to 5.13)	4.59 (4.01 to 5.17)
Hip Abduction-Left - Week 9	0.23 (-0.86 to 1.32)	1.19 (0.17 to 2.21)	0.38 (-0.25 to 1.01)	0.60 (0.08 to 1.11)
Hip Abduction-Left - Week 17	0.36 (-0.94 to 1.65)	-0.03 (-1.10 to 1.04)	0.74 (0.10 to 1.37)	0.36 (-0.20 to 0.92)
Hip Abduction-Left - Week 25	-0.49 (-1.85 to 0.87)	0.41 (-0.76 to 1.58)	0.52 (-0.13 to 1.16)	0.15 (-0.46 to 0.76)
Hip Abduction-Left - Week 33	0.18 (-1.16 to 1.51)	0.13 (-0.85 to 1.11)	0.26 (-0.47 to 0.99)	0.19 (-0.38 to 0.75)

Hip Abduction-Left - Week 41	-0.64 (-1.66 to 0.37)	-0.19 (-1.14 to 0.77)	0.59 (-0.08 to 1.27)	-0.06 (-0.56 to 0.44)
Hip Abduction-Left - Week 49	0.56 (-1.16 to 2.27)	-0.47 (-1.27 to 0.34)	0.55 (-0.29 to 1.38)	0.20 (-0.45 to 0.85)
Hip Abduction-Left - Week 57	-0.16 (-1.11 to 0.79)	-0.06 (-0.89 to 0.77)	0.62 (-0.06 to 1.29)	0.12 (-0.34 to 0.58)
Hip Abduction-Left - Week 65	-0.24 (-1.19 to 0.71)	-0.06 (-1.10 to 0.98)	0.86 (0.03 to 1.68)	0.18 (-0.35 to 0.71)
Hip Abduction-Left - Week 73	0.00 (-1.04 to 1.04)	0.31 (-0.81 to 1.43)	1.06 (0.07 to 2.04)	0.47 (-0.11 to 1.05)
Hip Abduction-Left - Week 81	-0.43 (-1.32 to 0.46)	0.17 (-0.91 to 1.26)	1.35 (0.63 to 2.06)	0.38 (-0.15 to 0.91)
Hip Abduction-Left - Week 89	0.37 (-0.64 to 1.38)	0.14 (-0.86 to 1.13)	0.78 (-0.01 to 1.57)	0.42 (-0.09 to 0.94)
Hip Abduction-Left - Week 97	-0.11 (-1.02 to 0.81)	-0.07 (-1.28 to 1.14)	0.40 (-0.25 to 1.05)	0.08 (-0.44 to 0.60)
Hip Abduction-Left - Week 110	-0.18 (-1.41 to 1.04)	-0.68 (-2.16 to 0.79)	0.22 (-0.92 to 1.36)	-0.22 (-0.93 to 0.48)
Hip Abduction-Left - Week 122	-0.09 (-2.41 to 2.23)	-0.13 (-1.61 to 1.36)	0.58 (-0.29 to 1.46)	0.15 (-0.65 to 0.95)
Hip Abduction-Left - Week 146	-1.24 (-4.04 to 1.55)	-0.26 (-2.36 to 1.84)	0.84 (-0.84 to 2.53)	-0.22 (-1.36 to 0.93)
Hip Abduction-Left - Week 170	-4.75 (-99999 to 99999)	-2.00 (-99999 to 99999)	-0.50 (-99999 to 99999)	-2.80 (-5.16 to -0.44)
Hip Abduction-Right - Baseline	4.14 (3.05 to 5.22)	5.39 (3.95 to 6.83)	4.53 (3.30 to 5.75)	4.69 (3.99 to 5.39)
Hip Abduction-Right - Week 9	0.56 (-0.84 to 1.97)	1.05 (-0.03 to 2.13)	0.03 (-0.61 to 0.67)	0.54 (-0.05 to 1.13)
Hip Abduction-Right - Week 17	0.56 (-0.62 to 1.75)	-0.51 (-1.67 to 0.66)	0.46 (-0.22 to 1.13)	0.18 (-0.39 to 0.74)
Hip Abduction-Right - Week 25	-0.31 (-1.44 to 0.83)	-0.23 (-1.57 to 1.11)	0.47 (-0.11 to 1.05)	-0.02 (-0.60 to 0.57)
Hip Abduction-Right - Week 33	0.42 (-1.09 to 1.93)	-0.80 (-1.89 to 0.29)	0.12 (-0.80 to 1.04)	-0.10 (-0.76 to 0.56)
Hip Abduction-Right - Week 41	-0.18 (-1.46 to 1.10)	-0.60 (-1.48 to 0.28)	0.22 (-0.60 to 1.03)	-0.19 (-0.74 to 0.35)
Hip Abduction-Right - Week 49	0.92 (-0.74 to 2.58)	-0.67 (-1.71 to 0.38)	0.33 (-0.38 to 1.03)	0.18 (-0.49 to 0.85)
Hip Abduction-Right - Week 57	0.13 (-0.91 to 1.16)	-0.63 (-1.66 to 0.41)	0.08 (-0.65 to 0.80)	-0.15 (-0.68 to 0.37)
Hip Abduction-Right - Week 65	0.19 (-0.82 to 1.20)	-0.17 (-1.52 to 1.18)	0.75 (0.10 to 1.40)	0.25 (-0.33 to 0.83)
Hip Abduction-Right - Week 73	0.12 (-0.87 to 1.10)	0.04 (-1.34 to 1.41)	0.73 (0.03 to 1.42)	0.29 (-0.28 to 0.87)
Hip Abduction-Right - Week 81	0.03 (-0.97 to 1.02)	-0.62 (-1.62 to 0.38)	0.69 (-0.01 to 1.38)	0.04 (-0.47 to 0.55)
Hip Abduction-Right - Week 89	0.08 (-0.72 to 0.87)	-0.44 (-1.41 to 0.54)	0.68 (0.08 to 1.28)	0.10 (-0.36 to 0.56)
Hip Abduction-Right - Week 97	0.05 (-0.96 to 1.06)	-0.20 (-1.43 to 1.03)	0.18 (-0.93 to 1.29)	0.01 (-0.60 to 0.62)
Hip Abduction-Right - Week 110	0.04 (-0.96 to 1.05)	-1.06 (-2.77 to 0.66)	-0.23 (-1.79 to 1.33)	-0.43 (-1.23 to 0.37)
Hip Abduction-Right - Week 122	-0.07 (-2.54 to 2.40)	-0.77 (-2.37 to 0.84)	0.52 (-0.52 to 1.56)	-0.09 (-0.97 to 0.79)
Hip Abduction-Right - Week 146	-1.10 (-3.32 to 1.12)	-1.44 (-2.89 to 0.01)	1.13 (0.25 to 2.01)	-0.37 (-1.32 to 0.59)
Hip Abduction-Right - Week 170	-4.30 (-99999 to 99999)	-1.75 (-99999 to 99999)	1.60 (-99999 to 99999)	-2.10 (-5.12 to 0.92)
Knee Extension-Left - Baseline	5.99 (4.01 to 7.98)	5.38 (4.01 to 6.74)	5.21 (3.53 to 6.88)	5.52 (4.60 to 6.43)
Knee Extension-Left - Week 9	-0.54 (-1.56 to 0.48)	1.20 (-0.24 to 2.64)	-0.16 (-0.81 to 0.49)	0.16 (-0.45 to 0.77)

Knee Extension-Left - Week 17	-0.88 (-2.29 to 0.53)	0.17 (-0.95 to 1.29)	-0.12 (-0.77 to 0.54)	-0.27 (-0.88 to 0.33)
Knee Extension-Left - Week 25	-1.66 (-2.98 to -0.34)	-0.14 (-1.37 to 1.09)	-0.38 (-0.84 to 0.07)	-0.72 (-1.33 to -0.11)
Knee Extension-Left - Week 33	-1.35 (-3.13 to 0.43)	-0.54 (-1.41 to 0.33)	-0.55 (-1.19 to 0.10)	-0.81 (-1.46 to -0.16)
Knee Extension-Left - Week 41	-1.53 (-3.47 to 0.41)	-0.87 (-1.84 to 0.11)	-0.67 (-1.14 to -0.21)	-1.00 (-1.66 to -0.34)
Knee Extension-Left - Week 49	-1.27 (-3.24 to 0.71)	-0.59 (-1.48 to 0.30)	-0.85 (-1.50 to -0.20)	-0.90 (-1.60 to -0.19)
Knee Extension-Left - Week 57	-1.67 (-3.50 to 0.16)	-0.77 (-1.80 to 0.27)	-0.73 (-1.79 to 0.32)	-1.06 (-1.80 to -0.31)
Knee Extension-Left - Week 65	-1.23 (-2.88 to 0.41)	-0.46 (-1.68 to 0.76)	-0.42 (-1.31 to 0.47)	-0.69 (-1.39 to 0.01)
Knee Extension-Left - Week 73	-1.78 (-3.77 to 0.21)	-0.39 (-1.85 to 1.07)	-0.02 (-0.57 to 0.53)	-0.69 (-1.48 to 0.10)
Knee Extension-Left - Week 81	-1.99 (-3.74 to -0.25)	-1.52 (-2.51 to -0.53)	-0.23 (-1.03 to 0.58)	-1.23 (-1.93 to -0.53)
Knee Extension-Left - Week 89	-2.16 (-3.98 to -0.33)	-1.45 (-2.46 to -0.43)	-0.27 (-1.16 to 0.61)	-1.28 (-2.00 to -0.56)
Knee Extension-Left - Week 97	-1.80 (-3.65 to 0.05)	-1.24 (-2.41 to -0.07)	-0.82 (-1.93 to 0.30)	-1.28 (-2.04 to -0.51)
Knee Extension-Left - Week 110	-2.28 (-4.26 to -0.30)	-1.79 (-3.16 to -0.42)	-1.89 (-3.18 to -0.60)	-1.98 (-2.82 to -1.15)
Knee Extension-Left - Week 122	-3.31 (-6.35 to -0.27)	-2.03 (-3.46 to -0.59)	-1.04 (-1.63 to -0.46)	-2.04 (-3.01 to -1.06)
Knee Extension-Left - Week 146	-3.36 (-8.02 to 1.31)	-0.83 (-1.93 to 0.26)	-0.57 (-1.50 to 0.36)	-1.63 (-3.13 to -0.12)
Knee Extension-Left - Week 170	-7.10 (-99999 to 99999)	-0.45 (-99999 to 99999)	-0.30 (-99999 to 99999)	-2.62 (-6.43 to 1.20)
Knee Extension-Right - Baseline	6.12 (4.21 to 8.04)	5.91 (4.43 to 7.39)	5.08 (3.31 to 6.85)	5.70 (4.76 to 6.64)
Knee Extension-Right - Week 9	-0.24 (-1.37 to 0.88)	1.02 (-0.49 to 2.53)	0.08 (-0.51 to 0.66)	0.28 (-0.34 to 0.90)
Knee Extension-Right - Week 17	-0.70 (-1.86 to 0.46)	-0.26 (-1.33 to 0.81)	-0.16 (-0.85 to 0.53)	-0.37 (-0.91 to 0.17)
Knee Extension-Right - Week 25	-1.27 (-2.92 to 0.37)	-0.71 (-2.06 to 0.64)	-0.21 (-0.82 to 0.40)	-0.72 (-1.42 to -0.03)
Knee Extension-Right - Week 33	-0.74 (-2.63 to 1.15)	-0.91 (-1.94 to 0.12)	-0.39 (-1.08 to 0.31)	-0.68 (-1.39 to 0.02)
Knee Extension-Right - Week 41	-1.16 (-3.13 to 0.80)	-1.07 (-2.19 to 0.05)	-0.28 (-0.96 to 0.40)	-0.83 (-1.54 to -0.12)
Knee Extension-Right - Week 49	-1.23 (-3.10 to 0.65)	-1.04 (-2.00 to -0.08)	-0.34 (-0.90 to 0.22)	-0.87 (-1.55 to -0.19)
Knee Extension-Right - Week 57	-1.44 (-3.16 to 0.28)	-1.16 (-2.24 to -0.08)	-0.69 (-1.45 to 0.06)	-1.11 (-1.79 to -0.42)
Knee Extension-Right - Week 65	-1.28 (-2.84 to 0.28)	-1.12 (-2.44 to 0.20)	-0.26 (-1.39 to 0.87)	-0.89 (-1.63 to -0.15)
Knee Extension-Right - Week 73	-1.57 (-3.28 to 0.14)	-1.24 (-2.55 to 0.08)	0.15 (-0.41 to 0.70)	-0.87 (-1.59 to -0.16)
Knee Extension-Right - Week 81	-1.82 (-3.37 to -0.26)	-1.97 (-3.11 to -0.84)	0.08 (-0.67 to 0.82)	-1.22 (-1.90 to -0.53)
Knee Extension-Right - Week 89	-2.05 (-3.88 to -0.22)	-1.80 (-2.83 to -0.76)	-0.21 (-0.87 to 0.45)	-1.35 (-2.05 to -0.64)
Knee Extension-Right - Week 97	-1.73 (-3.43 to -0.02)	-1.79 (-2.95 to -0.62)	-0.44 (-1.87 to 1.00)	-1.31 (-2.11 to -0.51)
Knee Extension-Right - Week 110	-2.21 (-3.84 to -0.58)	-2.05 (-3.48 to -0.63)	-1.42 (-2.72 to -0.12)	-1.89 (-2.67 to -1.11)
Knee Extension-Right - Week 122	-2.77 (-5.29 to -0.26)	-2.78 (-4.36 to -1.19)	-0.44 (-1.19 to 0.31)	-1.89 (-2.82 to -0.97)
Knee Extension-Right - Week 146	-3.21 (-7.01 to 0.58)	-1.13 (-2.61 to 0.34)	-0.56 (-1.86 to 0.75)	-1.66 (-2.97 to -0.35)

Knee Extension-Right - Week 170	-7.35 (-99999 to 99999)	-2.00 (-99999 to 99999)	-0.75 (-99999 to 99999)	-3.37 (-6.71 to -0.02)
Shoulder Abduction-Left - Baseline	3.55 (2.66 to 4.45)	4.24 (3.26 to 5.22)	3.44 (2.71 to 4.17)	3.75 (3.26 to 4.23)
Shoulder Abduction-Left - Week 9	-0.01 (-0.78 to 0.76)	0.58 (-0.21 to 1.38)	0.08 (-0.44 to 0.59)	0.21 (-0.17 to 0.60)
Shoulder Abduction-Left - Week 17	0.38 (-0.41 to 1.16)	-0.08 (-0.84 to 0.68)	0.11 (-0.32 to 0.54)	0.13 (-0.23 to 0.50)
Shoulder Abduction-Left - Week 25	-0.25 (-0.97 to 0.47)	0.08 (-0.78 to 0.94)	0.25 (-0.15 to 0.64)	0.03 (-0.35 to 0.41)
Shoulder Abduction-Left - Week 33	0.09 (-1.01 to 1.19)	-0.20 (-0.95 to 0.56)	0.12 (-0.11 to 0.35)	0.00 (-0.42 to 0.42)
Shoulder Abduction-Left - Week 41	0.14 (-0.94 to 1.23)	-0.22 (-0.90 to 0.46)	0.07 (-0.25 to 0.39)	-0.01 (-0.42 to 0.40)
Shoulder Abduction-Left - Week 49	0.36 (-0.97 to 1.69)	-0.29 (-0.90 to 0.31)	0.19 (-0.19 to 0.58)	0.09 (-0.39 to 0.56)
Shoulder Abduction-Left - Week 57	-0.05 (-0.88 to 0.77)	-0.49 (-1.11 to 0.13)	0.34 (-0.06 to 0.73)	-0.08 (-0.44 to 0.28)
Shoulder Abduction-Left - Week 65	-0.20 (-0.97 to 0.57)	0.03 (-0.96 to 1.02)	0.63 (0.26 to 0.99)	0.15 (-0.27 to 0.57)
Shoulder Abduction-Left - Week 73	-0.14 (-0.89 to 0.60)	0.13 (-0.72 to 0.97)	0.55 (0.19 to 0.90)	0.19 (-0.19 to 0.56)
Shoulder Abduction-Left - Week 81	-0.10 (-0.77 to 0.57)	-0.29 (-0.98 to 0.40)	0.58 (0.27 to 0.89)	0.07 (-0.25 to 0.40)
Shoulder Abduction-Left - Week 89	0.02 (-0.61 to 0.65)	-0.32 (-0.94 to 0.30)	0.23 (-0.12 to 0.57)	-0.03 (-0.33 to 0.27)
Shoulder Abduction-Left - Week 97	0.07 (-0.64 to 0.78)	-0.32 (-1.08 to 0.44)	0.33 (-0.30 to 0.96)	0.03 (-0.36 to 0.41)
Shoulder Abduction-Left - Week 110	-0.06 (-0.99 to 0.87)	-0.86 (-2.02 to 0.30)	-0.01 (-0.55 to 0.53)	-0.32 (-0.82 to 0.19)
Shoulder Abduction-Left - Week 122	-0.53 (-2.12 to 1.07)	-0.48 (-1.38 to 0.42)	0.24 (-0.22 to 0.69)	-0.22 (-0.76 to 0.31)
Shoulder Abduction-Left - Week 146	-0.89 (-3.08 to 1.31)	-0.48 (-2.23 to 1.27)	-0.16 (-0.64 to 0.33)	-0.51 (-1.28 to 0.26)
Shoulder Abduction-Left - Week 170	-3.75 (-99999 to 99999)	-0.90 (-99999 to 99999)	0.85 (-99999 to 99999)	-1.27 (-3.62 to 1.09)
Shoulder Abduction-Right - Baseline	3.80 (2.81 to 4.79)	4.33 (3.34 to 5.31)	3.46 (2.76 to 4.16)	3.86 (3.37 to 4.36)
Shoulder Abduction-Right - Week 9	-0.19 (-0.95 to 0.56)	0.22 (-0.50 to 0.95)	0.12 (-0.28 to 0.51)	0.05 (-0.30 to 0.40)
Shoulder Abduction-Right - Week 17	0.06 (-0.66 to 0.78)	-0.16 (-1.09 to 0.77)	0.19 (-0.15 to 0.54)	0.03 (-0.35 to 0.42)
Shoulder Abduction-Right - Week 25	-0.12 (-0.94 to 0.71)	0.08 (-1.01 to 1.17)	0.49 (-0.02 to 1.00)	0.16 (-0.31 to 0.62)
Shoulder Abduction-Right - Week 33	-0.16 (-1.26 to 0.94)	-0.54 (-1.32 to 0.24)	0.42 (0.11 to 0.73)	-0.09 (-0.53 to 0.35)
Shoulder Abduction-Right - Week 41	-0.20 (-1.29 to 0.89)	-0.47 (-1.17 to 0.23)	0.19 (-0.09 to 0.47)	-0.17 (-0.58 to 0.25)
Shoulder Abduction-Right - Week 49	0.35 (-1.48 to 2.18)	-0.43 (-1.02 to 0.16)	0.66 (0.23 to 1.10)	0.18 (-0.43 to 0.80)
Shoulder Abduction-Right - Week 57	-0.18 (-1.20 to 0.85)	-0.66 (-1.31 to -0.01)	0.33 (-0.09 to 0.75)	-0.19 (-0.60 to 0.23)
Shoulder Abduction-Right - Week 65	-0.10 (-1.10 to 0.90)	-0.16 (-0.98 to 0.67)	0.25 (-0.08 to 0.57)	-0.01 (-0.43 to 0.42)
Shoulder Abduction-Right - Week 73	-0.04 (-1.00 to 0.92)	-0.23 (-0.93 to 0.47)	0.58 (-0.01 to 1.17)	0.11 (-0.32 to 0.53)
Shoulder Abduction-Right - Week 81	0.06 (-0.93 to 1.06)	-0.30 (-1.01 to 0.41)	0.86 (0.26 to 1.46)	0.22 (-0.22 to 0.66)
Shoulder Abduction-Right - Week 89	0.10 (-0.91 to 1.11)	-0.52 (-1.11 to 0.07)	0.55 (0.10 to 0.99)	0.03 (-0.37 to 0.43)
Shoulder Abduction-Right - Week 97	-0.02 (-0.96 to 0.92)	-0.28 (-1.08 to 0.53)	0.46 (-0.27 to 1.19)	0.06 (-0.40 to 0.51)

Shoulder Abduction-Right - Week 110	-0.25 (-1.35 to 0.85)	-0.86 (-1.93 to 0.21)	-0.08 (-0.63 to 0.48)	-0.40 (-0.91 to 0.11)
Shoulder Abduction-Right - Week 122	-0.68 (-2.21 to 0.85)	-0.66 (-1.53 to 0.22)	0.14 (-0.51 to 0.79)	-0.36 (-0.91 to 0.18)
Shoulder Abduction-Right - Week 146	-1.50 (-3.96 to 0.96)	-0.75 (-1.89 to 0.39)	0.19 (-0.44 to 0.81)	-0.69 (-1.52 to 0.15)
Shoulder Abduction-Right - Week 170	-4.35 (-99999 to 99999)	-0.90 (-99999 to 99999)	-0.20 (-99999 to 99999)	-1.82 (-3.95 to 0.31)

Notes:

[115] - If no evaluable data collected, 99999 was entered instead.

[116] - If no evaluable data collected, 99999 was entered instead.

[117] - If no evaluable data collected, 99999 was entered instead.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum PF-06252616 (Domagrozumab) Concentration Versus Time Summary

End point title	Serum PF-06252616 (Domagrozumab) Concentration Versus Time Summary

End point description:

This analysis population was the PK Concentration Analysis Set consisting of all subjects who had received at least 1 dose of study medication in B5161004 and had at least 1 PF-06252616 (domagrozumab) concentration measured. N = x, y, z in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3.

End point type	Secondary

End point timeframe:

Weeks 1, 25, 49 and 73

End point values	Sequence 1	Sequence 2	Sequence 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	20	20	
Units: ng/mL				
arithmetic mean (standard deviation)				
Week 1 (N = 14, 17, 14)	145774.93 (± 56594.3925)	33.3529 (± 137.5176)	238433.36 (± 119862.330)	
Week 25 (N = 12, 12, 13)	355111.67 (± 90842.1052)	345943.67 (± 73922.3955)	488082.31 (± 199634.909)	
Week 49 (N = 7, 6, 8)	405812.43 (± 110320.246)	379259.33 (± 71128.3552)	459825.13 (± 49395.4262)	
Week 73 (N = 2, 2, 2)	401899.50 (± 3068.1363)	400176.00 (± 84223.4887)	401847.50 (± 164854.168)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-drug Antibodies (ADA) Development

End point title	Number of Subjects With Anti-drug Antibodies (ADA)

	Development

End point description:

The criterion for positive result of ADA samples was ADA titer >=1.88. The criterion for negative result of ADA samples was ADA titer <1.88.
This analysis population included all subjects who had received at least 1 dose of study medication.
N=x, y, z, t in the following table represents the number of evaluable subjects in Sequence groups 1, 2, 3 and Total.

End point type	Secondary

End point timeframe:

Weeks 1, 25, 49, 73 and Early Termination

End point values	Sequence 1	Sequence 2	Sequence 3	Total
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	20	20	59
Units: Subjects				
Week 1- Positive >=1.88(N=14,17,14,45)	0	0	0	0
Week 1 - Negative <1.88 (N=14,17,14,45)	14	17	14	45
Week 25 - Positive >=1.88 (N=12,12,13,37)	0	0	0	0
Week 25 -Negative <1.88 (N=12,12,13,37)	12	12	13	37
Week 49 - Positive >= 1.88 (N=7,6,8,21)	0	0	0	0
Week 49 -Negative <1.88 (N=7,6,8,21)	7	6	8	21
Week 73 - Positive >=1.88 (N=2,2,2,6)	0	0	0	0
Week 73 -Negative <1.88 (N=2,2,2,6)	2	2	2	6
Early Termination-Positive>=1.88(N=17,15,13,45)	0	0	0	0
Early Termination-Negative<1.88(N=17,15,13,45)	16	14	13	43

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

2 years

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Sequence 1

Reporting group description:

In study B5161002 (parent study) subjects randomized to Sequence group 1 received domagrozumab (PF-06252616) in a dose escalating fashion (5, 20 and 40 mg/kg), starting with the lowest dose in Period 1. At each dose level, dosing was administered over 2 hours by intravenous (IV) infusion every 4 weeks for a total of 16 weeks. In Period 2, subjects received domagrozumab (PF-06252616) at the maximum tolerated dose in Period 1 every 4 weeks for a total of 48 weeks. There was no pause between Period 1 and Period 2 (48 weeks each). In study B5161004 (OLE) subjects received domagrozumab 40 mg/kg (the maximum tolerated dose from B5161002) every 4 weeks. The OLE study reports subjects within the treatment assignment they received in the parent study.

Reporting group title	Sequence 2

Reporting group description:

In study B5161002 (parent study) subjects randomized to Sequence group 2 received domagrozumab (PF-06252616) in a dose escalating fashion (5, 20 and 40 mg/kg), starting with the lowest dose in Period 1. At each dose level, dosing was administered over 2 hours by IV infusion every 4 weeks for a total of 16 weeks. In Period 2, subjects received placebo. There was no pause between Period 1 and Period 2 (48 weeks each). In study B5161004 (OLE) subjects received domagrozumab 40 mg/kg (the maximum tolerated dose from B5161002) every 4 weeks. The OLE study reports subjects within the treatment assignment they received in the parent study.

Reporting group title	Sequence 3

Reporting group description:

In study B5161002 (parent study) subjects randomized to Sequence group 3 received placebo in Period 1 (48 weeks). In Period 2, subjects received domagrozumab (PF-06252616) in a dose escalating fashion (5, 20 and 40 mg/kg), starting with the lowest dose. At each dose level, dosing was administered over 2 hours by IV infusion every 4 weeks for a total of 16 weeks. There was no pause between Period 1 and Period 2 (48 weeks each). In study B5161004 (OLE) subjects received domagrozumab 40 mg/kg (the maximum tolerated dose from B5161002) every 4 weeks. The OLE study reports subjects within the treatment assignment they received in the parent study.

Reporting group title	Total

Reporting group description:

This is the sum of all subjects in the study

Serious adverse events	Sequence 1	Sequence 2	Sequence 3
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 19 (10.53%)	2 / 20 (10.00%)	1 / 20 (5.00%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Troponin increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences causally related to	0 / 1	0 / 0	0 / 0

treatment / all			
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (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
Fat embolism syndrome			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Ileus paralytic			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (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	Total		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 59 (8.47%)		
number of deaths (all causes)	1		
number of deaths resulting from	0		

adverse events			
Investigations			
Troponin increased			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fat embolism syndrome			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Ileus paralytic			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Volvulus			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Sequence 1	Sequence 2	Sequence 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 19 (78.95%)	17 / 20 (85.00%)	17 / 20 (85.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	3
General disorders and administration site conditions			
Gait inability			
subjects affected / exposed	2 / 19 (10.53%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	5
Pyrexia			
subjects affected / exposed	2 / 19 (10.53%)	3 / 20 (15.00%)	1 / 20 (5.00%)
occurrences (all)	3	3	1
Psychiatric disorders			
Intentional self-injury			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	2 / 20 (10.00%)
occurrences (all)	1	1	2
Fall			
subjects affected / exposed	4 / 19 (21.05%)	3 / 20 (15.00%)	6 / 20 (30.00%)
occurrences (all)	5	5	12
Hip fracture			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)

occurrences (all)	1	0	0
Ligament sprain			
subjects affected / exposed	2 / 19 (10.53%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Skin abrasion			
subjects affected / exposed	2 / 19 (10.53%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Spinal compression fracture			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Tibia fracture			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	2 / 20 (10.00%)
occurrences (all)	0	1	2
Investigations			
Troponin I increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Troponin increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	3 / 20 (15.00%)
occurrences (all)	0	1	4
Epistaxis			
subjects affected / exposed	3 / 19 (15.79%)	1 / 20 (5.00%)	2 / 20 (10.00%)
occurrences (all)	3	1	2
Nasal congestion			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	3 / 20 (15.00%)
occurrences (all)	2	1	4
Oropharyngeal pain			
subjects affected / exposed	0 / 19 (0.00%)	2 / 20 (10.00%)	3 / 20 (15.00%)

occurrences (all)	0	2	3
Rhinorrhoea			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	2 / 20 (10.00%)
occurrences (all)	0	1	2
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 19 (26.32%)	1 / 20 (5.00%)	5 / 20 (25.00%)
occurrences (all)	8	1	12
Hypoaesthesia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	2 / 19 (10.53%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	2
Constipation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Diarrhoea			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	3 / 20 (15.00%)
occurrences (all)	1	0	3
Nausea			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Toothache			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	3 / 19 (15.79%)	2 / 20 (10.00%)	3 / 20 (15.00%)
occurrences (all)	6	2	3
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 19 (10.53%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	2
Pain in extremity			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Tendon disorder			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Insulin resistance			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Ear infection			
subjects affected / exposed	0 / 19 (0.00%)	2 / 20 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Fungal skin infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	1 / 19 (5.26%)	4 / 20 (20.00%)	0 / 20 (0.00%)
occurrences (all)	1	4	0
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	4 / 19 (21.05%)	3 / 20 (15.00%)	4 / 20 (20.00%)
occurrences (all)	4	3	5
Pharyngitis streptococcal			

subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	3
Respiratory tract infection viral			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 19 (15.79%)	0 / 20 (0.00%)	2 / 20 (10.00%)
occurrences (all)	4	0	2
Viral infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Total		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 59 (83.05%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	2		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
General disorders and administration site conditions			
Gait inability			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	5		

Pyrexia subjects affected / exposed occurrences (all)	6 / 59 (10.17%) 7		
Psychiatric disorders Intentional self-injury subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) Fall subjects affected / exposed occurrences (all) Hip fracture subjects affected / exposed occurrences (all) Ligament sprain subjects affected / exposed occurrences (all) Skin abrasion subjects affected / exposed occurrences (all) Spinal compression fracture subjects affected / exposed occurrences (all) Tibia fracture subjects affected / exposed occurrences (all)	 4 / 59 (6.78%) 4 13 / 59 (22.03%) 22 1 / 59 (1.69%) 1 2 / 59 (3.39%) 2 3 / 59 (5.08%) 3 2 / 59 (3.39%) 2 3 / 59 (5.08%) 3		
Investigations Troponin I increased subjects affected / exposed occurrences (all) Troponin increased subjects affected / exposed occurrences (all)	 1 / 59 (1.69%) 1 1 / 59 (1.69%) 1		

Cardiac disorders Cardiomyopathy subjects affected / exposed occurrences (all)	 1 / 59 (1.69%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	 4 / 59 (6.78%) 5 6 / 59 (10.17%) 6 5 / 59 (8.47%) 7 5 / 59 (8.47%) 5 3 / 59 (5.08%) 3		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Hypoaesthesia subjects affected / exposed occurrences (all)	 11 / 59 (18.64%) 21 1 / 59 (1.69%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	 1 / 59 (1.69%) 1 4 / 59 (6.78%) 4 2 / 59 (3.39%) 2		

Diarrhoea subjects affected / exposed occurrences (all)	4 / 59 (6.78%) 4		
Nausea subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2		
Toothache subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2		
Vomiting subjects affected / exposed occurrences (all)	8 / 59 (13.56%) 11		
Skin and subcutaneous tissue disorders Urticaria subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	4 / 59 (6.78%) 4		
Pain in extremity subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2		
Tendon disorder subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1		
Metabolism and nutrition disorders Insulin resistance subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2		
Infections and infestations Conjunctivitis subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1		
Ear infection subjects affected / exposed	2 / 59 (3.39%)		

occurrences (all)	2		
Fungal skin infection			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Influenza			
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	5		
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	11 / 59 (18.64%)		
occurrences (all)	12		
Pharyngitis streptococcal			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	3		
Respiratory tract infection viral			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	5 / 59 (8.47%)		
occurrences (all)	6		
Viral infection			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was terminated prematurely due to insufficient efficacy and not due to safety reasons.

Notes: