



## Clinical trial results:

**A phase III, randomized, double blind, placebo-controlled clinical study to assess the efficacy and safety of GSK2402968 in subjects with Duchenne muscular dystrophy.**

### Summary

EudraCT number	2010-020069-26
Trial protocol	DE FR NL BE IT PL CZ ES NO DK HU Outside EU/EEA
Global end of trial date	28 June 2013

### Results information

Result version number	v1 (current)
This version publication date	26 October 2019
First version publication date	26 October 2019

### Trial information

#### Trial identification

Sponsor protocol code	DMD114044
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01254019
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Centre, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@GSK.com
Scientific contact	GSK Response Centre, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@GSK.com

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000746-PIP01-04
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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	28 June 2013
Is this the analysis of the primary completion data?	No

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Global end of trial reached?	Yes
Global end of trial date	28 June 2013
Was the trial ended prematurely?	No

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Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the efficacy of subcutaneous 6 mg/kg GSK2402968 versus placebo administered over 48 weeks in ambulant participants with DMD.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Months
Independent data monitoring committee (IDMC) involvement?	Yes

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Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Brazil: 18
Country: Number of subjects enrolled	Canada: 20
Country: Number of subjects enrolled	Chile: 7
Country: Number of subjects enrolled	Czech Republic: 7
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Italy: 26
Country: Number of subjects enrolled	Japan: 14
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Norway: 3
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Russian Federation: 8
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	Turkey: 5

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Worldwide total number of subjects	186
EEA total number of subjects	99

Notes:

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### Subjects enrolled per age group

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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)	169
Adolescents (12-17 years)	17
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

This study was conducted across 44 centers in 19 countries from 02 December 2010 to 28 June 2013.

### Pre-assignment

Screening details:

A total of 186 participants were randomized which included males with a maximum age of 16 years, no adults were included in this study.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	Placebo
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Arm description:

Participants received single dose of matching placebo sterile solution for subcutaneous injection preferably in the morning over the 48 week treatment period.

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

Dosage and administration details:

Placebo was administered as a single dose sterile solution via subcutaneous route preferably in the morning over the 48 week treatment period.

<b>Arm title</b>	GSK2402968 6mg/kg/week
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Arm description:

Participants received single dose of GSK2402968 6 milligrams per kilogram per week (mg/kg/week) subcutaneous injection preferably in the morning over the 48 week treatment period.

Arm type	Experimental
Investigational medicinal product name	GSK2402968
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

GSK2402968 was administered as a single dose of GSK2402968 6 milligrams per kilogram per week (mg/kg/week) via subcutaneous route preferably in the morning over the 48 week treatment period.

<b>Number of subjects in period 1</b>	Placebo	GSK2402968 6mg/kg/week
Started	61	125
Completed	60	121
Not completed	1	4
Consent withdrawn by subject	-	2
Adverse Event	-	2
Protocol deviation	1	-

## Baseline characteristics

### Reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received single dose of matching placebo sterile solution for subcutaneous injection preferably in the morning over the 48 week treatment period.	
Reporting group title	GSK2402968 6mg/kg/week
Reporting group description:	
Participants received single dose of GSK2402968 6 milligrams per kilogram per week (mg/kg/week) subcutaneous injection preferably in the morning over the 48 week treatment period.	

Reporting group values	Placebo	GSK2402968 6mg/kg/week	Total
Number of subjects	61	125	186
Age categorical			
Units: Subjects			
Overall Participants	61	125	186
Age Continuous			
Units: Years			
arithmetic mean	8.0	8.3	
standard deviation	± 2.37	± 2.43	-
Sex: Female, Male			
Units: Subjects			
Female	0	0	0
Male	61	125	186
Race/Ethnicity, Customized			
Units: Subjects			
African American/African Heritage	1	0	1
Asian - Central/South Asian Heritage	1	3	4
Asian - East Asian Heritage	3	6	9
Asian - Japanese Heritage	5	9	14
Asian - South East Asian Heritage	0	2	2
White - Arabic/North African Heritage	4	5	9
White - White/Caucasian/European Heritage	46	95	141
White - Mixed Race	0	1	1
Mixed Race	1	4	5

## End points

### End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received single dose of matching placebo sterile solution for subcutaneous injection preferably in the morning over the 48 week treatment period.	
Reporting group title	GSK2402968 6mg/kg/week
Reporting group description:	
Participants received single dose of GSK2402968 6 milligrams per kilogram per week (mg/kg/week) subcutaneous injection preferably in the morning over the 48 week treatment period.	

### Primary: Change from Baseline in muscle function using the 6 Minute Walking Distance (6MWD) test assessed at Week 48

End point title	Change from Baseline in muscle function using the 6 Minute Walking Distance (6MWD) test assessed at Week 48
End point description:	
During the 6MWD, participants were asked to walk, at their own preferred speed, up and down a fixed distance until they were told to stop after 6 minutes. The participants were warned of the time and were told that they may stop earlier if they feel unable to continue. The total distance walked within 6 minutes (or until the participant stopped in case of early termination of the test), the 6MWD, was recorded in meters as well as any falls. Baseline was defined as participants randomization assessment at Visit 3 (Day 0). Change from Baseline was calculated by subtracting the Baseline value from the value at Week 48.	
The intent-to-treat (ITT) population comprised all participants who received atleast one dose of study medication and for whom atleast one post-Baseline efficacy assessment was available. A mixed model with repeated measures (MMRM) analysis was performed, including all available data at each visit.	
End point type	Primary
End point timeframe:	
Baseline (Day 0) and Week 48	

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59 <sup>[1]</sup>	117 <sup>[2]</sup>		
Units: Meters				
least squares mean (standard error)	-52.65 ( $\pm$ 10.423)	-42.32 ( $\pm$ 7.378)		

Notes:

[1] - ITT Population

[2] - ITT Population

### Statistical analyses

Statistical analysis title	GSK2402968 6mg/kg/week Vs Placebo
Comparison groups	Placebo v GSK2402968 6mg/kg/week

Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.415 <sup>[3]</sup>
Method	Mixed Effect Model for Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	10.334
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.645
upper limit	35.312

Notes:

[3] - Statistical significance was assessed at the 5% level.

### Secondary: Change from Baseline in the linearized North Star Ambulatory Assessment (NSAA) total score at Week 48

End point title	Change from Baseline in the linearized North Star Ambulatory Assessment (NSAA) total score at Week 48
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End point description:

The NSAA is a functional scale devised from the Hammersmith Scale of Motor Ability specifically for use in ambulant children with Duchenne muscular dystrophy (DMD). It consists of 17 activities graded 0 (unable to perform), 1 (performs with modifications), 2 (normal movement). The scale assesses activities required to remain functionally ambulant (e.g. rise from the floor), activities that can be difficult even early in the disease (e.g. standing on heels) and activities that are known to progressively deteriorate over time (stand from a chair, walk). NSAA total score was achieved by adding the responses of all activities, ranging from 0 to 34, with a score of 34 implying normal function and lower score implying more severe symptoms.

Baseline was defined as participants randomization assessment at Visit 3 (Day 0). Change from Baseline was calculated by subtracting the Baseline value from the value at Week 48. A positive change from Baseline indicated improvement.

End point type	Secondary
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End point timeframe:

Baseline (Day 0) and Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58 <sup>[4]</sup>	117 <sup>[5]</sup>		
Units: Scores on a scale				
least squares mean (standard error)	-6.7 (± 1.43)	-7.2 (± 1.01)		

Notes:

[4] - ITT Population. MMRM analysis was performed, including all available data at each visit.

[5] - ITT Population. MMRM analysis was performed, including all available data at each visit.

### Statistical analyses

Statistical analysis title	GSK2402968 6mg/kg/week Vs Placebo
Comparison groups	Placebo v GSK2402968 6mg/kg/week



Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.757
Method	Mixed Effect Model for Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.95
upper limit	2.88

### Secondary: Change from Baseline in the 4 stair climb (ascent) velocity at Week 48

End point title	Change from Baseline in the 4 stair climb (ascent) velocity at Week 48
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#### End point description:

The participant was asked to ascend four steps. Time was recorded with a stopwatch from the initiation of movement until the participant stood on the fourth step. A flight of steps with handrail was used for this test. Number of stairs ascended per second was calculated as 4 divided by the time to ascend 4 complete stairs.

Baseline was defined as participants randomization assessment at Visit 3 (Day 0). Change from Baseline was calculated by subtracting the Baseline value from the value at Week 48.

End point type	Secondary
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#### End point timeframe:

Baseline (Day 0) and Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55 <sup>[6]</sup>	111 <sup>[7]</sup>		
Units: Stairs per second				
least squares mean (standard error)	-0.12 (± 0.049)	-0.14 (± 0.035)		

#### Notes:

[6] - ITT Population. MMRM analysis was performed, including all available data at each visit.

[7] - ITT Population. MMRM analysis was performed, including all available data at each visit.

### Statistical analyses

Statistical analysis title	GSK2402968 6mg/kg/week Vs Placebo
Comparison groups	Placebo v GSK2402968 6mg/kg/week

Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.718
Method	Mixed Effect Model for Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.021
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.137
upper limit	0.095

## Secondary: Change from Baseline in the 10-meter walk/run velocity at Week 48

End point title	Change from Baseline in the 10-meter walk/run velocity at Week 48
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### End point description:

The participant was instructed to perform the test bare foot. No aids or orthoses were allowed. The participant was asked to traverse a marked 10-meter measured walkway as quickly as he safely could. Time was recorded to one tenth of a second with a stopwatch from when his first foot crossed the start line until when the second foot crossed the finish line.

Baseline was defined as participant's randomization assessment at visit 3 (Day 0). Change from Baseline was calculated by subtracting the Baseline value from the value at Week 48.

End point type	Secondary
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### End point timeframe:

Baseline (Day 0) and Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58 <sup>[8]</sup>	117 <sup>[9]</sup>		
Units: Meters per second				
least squares mean (standard error)	-0.20 (± 0.050)	-0.21 (± 0.035)		

### Notes:

[8] - ITT Population. MMRM analysis was performed, including all available data at each visit.

[9] - ITT Population. MMRM analysis was performed, including all available data at each visit.

## Statistical analyses

Statistical analysis title	GSK2402968 6mg/kg/week Vs Placebo
Comparison groups	Placebo v GSK2402968 6mg/kg/week

Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.881
Method	Mixed Effect Model for Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.009
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.129
upper limit	0.111

## Secondary: Change from Baseline in the timed function test Rise from floor at Week 48

End point title	Change from Baseline in the timed function test Rise from floor at Week 48
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End point description:

The participant stood from a standardized supine position as quickly as possible when told to go. Time was recorded with a stopwatch from the initiation of movement until the assumption of upright standing. No aids or orthoses were allowed.

Baseline was defined as participants randomization assessment at Visit 3 (Day 0). Change from Baseline was calculated by subtracting the Baseline value from the value at Week 48.

End point type	Secondary
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End point timeframe:

Baseline (Day 0) and Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44 <sup>[10]</sup>	91 <sup>[11]</sup>		
Units: Seconds				
least squares mean (standard error)	7.48 (± 2.080)	6.36 (± 1.463)		

Notes:

[10] - ITT Population. MMRM analysis was performed, including all available data at each visit.

[11] - ITT Population. MMRM analysis was performed, including all available data at each visit.

## Statistical analyses

Statistical analysis title	GSK2402968 6mg/kg/week Vs Placebo
Comparison groups	Placebo v GSK2402968 6mg/kg/week
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.658 <sup>[12]</sup>
Method	Mixed Effect Model for Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-1.115

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.097
upper limit	3.866

Notes:

[12] - Negative difference compared to placebo represents benefit over placebo.

## Secondary: Change from Baseline in the 4 stair climb (descent) velocity at Week 48

End point title	Change from Baseline in the 4 stair climb (descent) velocity at Week 48
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End point description:

The participant was asked to descend four steps. Time was recorded with a stopwatch from the initiation of movement until the participant stood on the fourth step.

Baseline was defined as participants randomization assessment at Visit 3 (Day 0). Change from Baseline was calculated by subtracting the Baseline value from the value at Week 48.

End point type	Secondary
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End point timeframe:

Baseline (Day 0) and Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55 <sup>[13]</sup>	109 <sup>[14]</sup>		
Units: Stairs per second				
least squares mean (standard error)	-0.15 (± 0.052)	-0.11 (± 0.037)		

Notes:

[13] - ITT Population. MMRM analysis was performed, including all available data at each visit.

[14] - ITT Population. MMRM analysis was performed, including all available data at each visit.

## Statistical analyses

Statistical analysis title	GSK2402968 6mg/kg/week Vs Placebo
Comparison groups	Placebo v GSK2402968 6mg/kg/week
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.513 <sup>[15]</sup>
Method	Mixed Effect Model for Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	0.041
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.082
upper limit	0.164

Notes:

[15] - Positive difference compared to placebo represents benefit over placebo

## Secondary: Change from Baseline in muscle strength (total score) at Week 48

End point title	Change from Baseline in muscle strength (total score) at Week 48
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End point description:

Muscle strength was recorded by handheld myometry using a micro force evaluation testing 2 (FET2) myometer. Upper and lower limb proximal muscles were evaluated including knee flexors, knee extensors, elbow flexors, elbow extensors, shoulder abductors and hip flexors. The muscle strength total score (pounds) was the sum of the 12 individual muscle strength tests.

Baseline was defined as participants randomization assessment at Visit 3 (Day 0). Change from Baseline was calculated by subtracting the Baseline value from the value at Week 48.

End point type	Secondary
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End point timeframe:

Baseline (Day 0) and Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58 <sup>[16]</sup>	118 <sup>[17]</sup>		
Units: lbs				
least squares mean (standard error)	-1.21 (± 2.729)	-2.18 (± 1.926)		

Notes:

[16] - ITT Population. MMRM analysis was performed, including all available data at each visit.

[17] - ITT Population. MMRM analysis was performed, including all available data at each visit.

## Statistical analyses

Statistical analysis title	GSK2402968 6mg/kg/week Vs Placebo
Comparison groups	Placebo v GSK2402968 6mg/kg/week
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.769 <sup>[18]</sup>
Method	Mixed Effect Model for Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.965
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.446
upper limit	5.516

Notes:

[18] - Positive difference compared to placebo represents benefit over placebo

## Secondary: Kaplan-Meier Estimates for Time to loss of ambulation

End point title	Kaplan-Meier Estimates for Time to loss of ambulation
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End point description:

All participants were ambulant when entered into the study; however they could have become non-ambulant at some time during the study. The date was recorded and the variable time to loss of ambulation was calculated as: time to loss of ambulation = date of loss of ambulation – date of first dose. Median and interquartile range i.e. 1st and 3rd quartile is presented. 99999 indicates calculation of statistics was not possible due to insufficient events.

End point type	Secondary
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End point timeframe:

Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61 <sup>[19]</sup>	125 <sup>[20]</sup>		
Units: Days				
median (inter-quartile range (Q1-Q3))	99999 (99999 to 99999)	99999 (390.0 to 99999)		

Notes:

[19] - ITT Population

[20] - ITT Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants who experienced accidental falls during 6MWD assessments at Week 48

End point title	Number of participants who experienced accidental falls during 6MWD assessments at Week 48
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End point description:

The number of accidental falls occurring during the 6MWD were counted. Data has been presented for the number of participants who experienced accidental falls (from 0 to 1) during the 6MWD assessment. Only those participants with data available at the indicated time points were analyzed.

End point type	Secondary
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End point timeframe:

Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53 <sup>[21]</sup>	103 <sup>[22]</sup>		
Units: Participants				
Number of falls=0	48	102		
Number of falls=1	5	1		

Notes:

[21] - ITT Population

[22] - ITT Population

## Statistical analyses

**Secondary: Change from Baseline in creatine kinase serum concentrations at Week 48**

End point title	Change from Baseline in creatine kinase serum concentrations at Week 48
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## End point description:

Creatine kinase is a muscle-specific enzyme; its level in serum is considered to reflect the extent of muscle damage. In the blood samples drawn to this purpose, the serum level of creatine kinase were measured.

Baseline was defined as participants randomization assessment at Visit 3 (Day 0). Change from Baseline was calculated by subtracting the Baseline value from the value at Week 48.

End point type	Secondary
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## End point timeframe:

Baseline (Day 0) and Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60 <sup>[23]</sup>	118 <sup>[24]</sup>		
Units: International units per liter				
least squares mean (standard error)	-1228.5 (± 500.59)	-5273.5 (± 359.05)		

## Notes:

[23] - ITT population. MMRM analysis was performed, including all available data at each visit.

[24] - ITT population. MMRM analysis was performed, including all available data at each visit.

**Statistical analyses**

<b>Statistical analysis title</b>	GSK2402968 6mg/kg/week Vs Placebo
Comparison groups	Placebo v GSK2402968 6mg/kg/week
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 <sup>[25]</sup>
Method	Mixed Effect Model for Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-4044.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5232.21
upper limit	-2857.77

## Notes:

[25] - No adjustment for multiplicity was made, so p-values should not be used to make conclusions with regards to statistical significance.

**Secondary: Change from Baseline in Pulmonary Function test Forced vital capacity (FVC) and Forced expiratory volume in 1 second (FEV1) at Week 48**

End point title	Change from Baseline in Pulmonary Function test Forced vital capacity (FVC) and Forced expiratory volume in 1 second
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## End point description:

The FEV1 is the volume of air forcefully exhaled in 1 second, whereas the FVC is the volume of air that can be maximally forcefully exhaled using non-invasive spirometry was conducted to determine actual and percentage values for FVC and FEV1. Baseline was defined as participants randomization assessment at Visit 3 (Day 0). Change from Baseline was calculated by subtracting the Baseline value from the value at Week 48. Only those participants available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Secondary
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End point timeframe:

Baseline (Day 0) and Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61 <sup>[26]</sup>	125 <sup>[27]</sup>		
Units: Liters				
arithmetic mean (standard deviation)				
FVC at Week 48; n=58, 121	0.118 (± 0.1847)	0.087 (± 0.2337)		
FEV1 at Week 48; n=55, 116	0.126 (± 0.2530)	0.049 (± 0.2997)		

Notes:

[26] - ITT Population

[27] - ITT Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of participants with Identified Mutation: DMD Exon 51 skip (upon muscle biopsies) at Week 48**

End point title	Number of participants with Identified Mutation: DMD Exon 51 skip (upon muscle biopsies) at Week 48
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## End point description:

Biopsies were taken from their tibialis anterior muscle and few were taken from quadriceps. Total muscle ribonucleic acid (RNA) was isolated from muscle tissue sections and was analyzed by reverse transcriptase polymer chain reaction (RT-PCR). RT-PCR analysis focused on the area flanking the targeted exon 51 was performed to detect specific exon 51 skipping in muscle. Depending on the participants mutation different sets of DMD-gene specific RT and PCR primers were used. Sequence analysis was performed on isolated PCR products to confirm specific exon 51 skip band detection. Only those participants with data available at the indicated time points were analyzed.

End point type	Secondary
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End point timeframe:

Week 48



End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59 <sup>[28]</sup>	119 <sup>[29]</sup>		
Units: Participants				
DMD Exon 51 skip, Band detected	48	106		
DMD Exon 51 skip, No Band detected	9	9		
DMD Exon 51 skip, No result	0	2		
DMD Exon 51 skip, Not analyzed	2	2		

Notes:

[28] - ITT Population

[29] - ITT Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Pediatric Quality of Life (PedsQL) Total Score at Week 48

End point title	Change from Baseline in Pediatric Quality of Life (PedsQL) Total Score at Week 48
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End point description:

PedsQL version 3.0 scale is used to measure pediatric quality of life in children with neuromuscular disorders. The 25-item PedsQL encompasses 3 scales About My/My Childs Neuromuscular Disease (17 items), Communication (3 items), About Our Family Resources (5 items). A 5-point response scale is utilized (where 0=never a problem; 4=almost always a problem). It was assessed both by child and parent. PedsQL total score was calculated by reverse scoring individual items and linearly transforming the score to a 0-100 scale, where higher scores indicated better health-related quality of life. To reverse score individual items, the 0-4 scale items were transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, and 4=0. Total score was then calculated as sum of items divided by number of items answered. Change from Baseline was calculated by subtracting the Baseline value from the value at Week 48. A positive change from Baseline indicated improvement.

End point type	Secondary
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End point timeframe:

Baseline (Day 0) and Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61 <sup>[30]</sup>	125 <sup>[31]</sup>		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Assessor child at week 48; n=57, 114	0.52 (± 11.313)	1.36 (± 11.360)		
Assessor parent at week 48; n=58, 117	-0.11 (± 11.064)	-1.19 (± 11.269)		

Notes:

[30] - ITT population. Only those participants available at the specified time points were analyzed.

[31] - ITT population. Only those participants available at the specified time points were analyzed.

## Statistical analyses

No statistical analyses for this end point

**Secondary: Change from Baseline in Pulmonary Function test peak cough flow (PCF) and peak flow (PF) at Week 48**

End point title	Change from Baseline in Pulmonary Function test peak cough flow (PCF) and peak flow (PF) at Week 48
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End point description:

The PF also called peak expiratory flow rate (PEFR) is a participants maximum speed of expiration, as measured with a peak flow meter, a small, hand-held device used to monitor a participants ability to breathe out air. PCF was measured for participants wearing a nose clip and performing a maximum cough into a pocket peak flow meter. Baseline was defined as participants randomization assessment at Visit 3 (Day 0). Change from Baseline was calculated by subtracting the Baseline value from the value at Week 48.

End point type	Secondary
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End point timeframe:

Baseline (Day 0) and Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61 <sup>[32]</sup>	125 <sup>[33]</sup>		
Units: Liters per minute				
arithmetic mean (standard deviation)				
PF at Week 48; n=59, 121	25.810 (± 41.5342)	11.603 (± 42.6964)		
PCF at Week 48; n=59, 120	22.7 (± 42.46)	10.7 (± 45.04)		

Notes:

[32] - ITT population. Only those participants available at the specified time points were analyzed.

[33] - ITT population. Only those participants available at the specified time points were analyzed.

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of participants who showed improvement on Clinician Global Impression of Improvement (CGI-I) scale at Week 48**

End point title	Number of participants who showed improvement on Clinician Global Impression of Improvement (CGI-I) scale at Week 48
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End point description:

The CGI-I is scored based on the clinician's reflection of the participant's current overall clinical condition compared to the overall clinical condition just prior to the initiation of medication use (i.e., the period prior to Randomization). The CGI-I is rated without regard to the clinician's belief that any clinical changes are or are not due to medication and without consideration of the etiology of the symptoms. The CGI-I is measured on a 7-point Likert scale (where 1=very much improved, 2=much improved, 3=minimally improved, 4=no change, 5=minimally worse, 6=much worse, 7=very much worse). The score ranged from 1-7, where lower score indicated more improvement and higher score indicated less improvement.

End point type	Secondary
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End point timeframe:

Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57 <sup>[34]</sup>	116 <sup>[35]</sup>		
Units: Participants				
Very much improved	0	3		
Much improved	1	9		
Minimally improved	2	23		
No change	27	41		
Minimally worse	20	30		
Much worse	6	10		
Very much worse	1	0		

Notes:

[34] - ITT population. Only those participants with data available at specified time points were analyzed

[35] - ITT population. Only those participants with data available at specified time points were analyzed

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Health Utilities Index (HUI) Scores at Week 48

End point title	Change from Baseline in Health Utilities Index (HUI) Scores at Week 48
End point description:	
A 15-item HUI questionnaire assessed Health-related quality of life (HRQoL). Responses from 15-item HUI were used to quantify HRQoL according to 2 health status classification systems, HUI Mark 2 (HUI2) and HUI Mark 3 (HUI3). HUI2 assessed 7 HRQoL dimensions: sensation, mobility, emotion, cognition, self care, pain and fertility. HUI3 assessed 8 HRQoL dimensions: vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain. Both HUI2 (range from -0.03 to 1.0) and HUI3 (range from -0.36 to 1.0) utility scores were calculated using algorithms incorporating community-derived preference weights. A utility value of 1.0 represented perfect health and a utility value of 0.0 represented death. Lowest possible HUI2 score was -0.03 and for HUI3 score was -0.36, where scores less than 0 represented health states considered worse than death. Change from Baseline was calculated by subtracting Baseline value from Week 48 value. A positive change from Baseline indicated improvement.	
End point type	Secondary
End point timeframe:	
Baseline (Randomization Visit, Day 0) and Week 48	

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61 <sup>[36]</sup>	125 <sup>[37]</sup>		
Units: Scores on a scale				
least squares mean (standard error)				
HUI2 at Week 48; n=53, 112	-0.052 (± 0.0190)	-0.023 (± 0.0133)		
HUI3 at Week 48; n=56, 116	-0.061 (± 0.0266)	-0.056 (± 0.0188)		

Notes:

[36] - ITT Population. MMRM analysis was performed, including all available data at each visit.

[37] - ITT Population. MMRM analysis was performed, including all available data at each visit.

## Statistical analyses

<b>Statistical analysis title</b>	GSK2402968 6mg/kg/week Vs Placebo, HUI2 at Week 48
Comparison groups	Placebo v GSK2402968 6mg/kg/week
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.207 <sup>[38]</sup>
Method	Mixed Model for Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	0.0288
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0161
upper limit	0.0738

Notes:

[38] - No adjustment for multiplicity was made, so p-values should not be used to make conclusions with regards to statistical significance.

<b>Statistical analysis title</b>	GSK2402968 6mg/kg/week Vs Placebo, HUI3 at Week 48
Comparison groups	Placebo v GSK2402968 6mg/kg/week
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.88 <sup>[39]</sup>
Method	Mixed Model for Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	0.0048
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.058
upper limit	0.0676

Notes:

[39] - No adjustment for multiplicity was made, so p-values should not be used to make conclusions with regards to statistical significance.

## Secondary: Number of participants with adverse events (AE) and severe adverse events (SAE)

End point title	Number of participants with adverse events (AE) and severe adverse events (SAE)
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End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. An SAE is any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect.

End point type	Secondary
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End point timeframe:

Up to Follow-up (Week 68)

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61 <sup>[40]</sup>	125 <sup>[41]</sup>		
Units: Participants				
Any AE	58	123		
Any SAE	5	13		

Notes:

[40] - Safety Population comprised of all participants who received at least one dose of study medication

[41] - Safety Population comprised of all participants who received at least one dose of study medication

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with vital sign data for systolic blood pressure (SBP) and diastolic blood pressure (DBP) and heart rate (HR) of potential clinical concern (PCC) at any visit post-Baseline

End point title	Number of participants with vital sign data for systolic blood pressure (SBP) and diastolic blood pressure (DBP) and heart rate (HR) of potential clinical concern (PCC) at any visit post-Baseline
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End point description:

Blood pressure SBP, DBP and HR were recorded after five minutes of rest in a semi-supine position. The following changes from Baseline (Day 0) in vital signs were considered to be of potential clinical concern: DBP was defined as high (increase from Baseline  $\geq 20$  and  $\geq 40$  millimeters of mercury [mmHg] and low (decrease from Baseline  $\geq 20$  and  $\geq 40$  mmHg), SBP high (increase from Baseline  $\geq 10$  and  $\geq 20$  mmHg and low (decrease from Baseline  $\geq 10$  and  $\geq 20$  mmHg) and for HR high (increase from Baseline  $\geq 20$  and  $\geq 40$  beats per minute [bpm] and low (decrease from Baseline  $\geq 20$  and  $\geq 40$  bpm). Only those parameters for which a value of PCC was reported at any visit post-Baseline is presented.

End point type	Secondary
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End point timeframe:

Up to Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61 <sup>[42]</sup>	125 <sup>[43]</sup>		
Units: Participants				
DBP, High at any visit post-Baseline	22	52		
HR, low at any visit post-Baseline	19	49		
HR, high at any visit post-Baseline	18	32		
SBP, low at any visit post-Baseline	8	7		
SBP, high at any visit post-Baseline	28	72		

Notes:

[42] - Safety Population

[43] - Safety Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with abnormal-clinically significant Electrocardiogram (ECG) findings at any visit post-Baseline

End point title	Number of participants with abnormal-clinically significant Electrocardiogram (ECG) findings at any visit post-Baseline
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End point description:

ECG measurements were carried out and the clinical interpretation of the ECG by the investigator was recorded as normal, abnormal but not clinically significant and abnormal clinically significant. The PCC ranges include, QT interval corrected for heart rate by Bazett's formula (QTcB) or QT interval corrected for heart rate by Fridericia's formula (QTcF) >450 milliseconds and any increase from Baseline of QTcB or QTcF. Participants were categorized as abnormal clinically significant based on the investigator's judgment and PCC ranges. Data has been presented for number of participants with abnormal clinically significant findings at any visit post-Baseline.

End point type	Secondary
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End point timeframe:

Up to Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61 <sup>[44]</sup>	125 <sup>[45]</sup>		
Units: Participants	0	5		

Notes:

[44] - Safety Population

[45] - Safety Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with hematology parameters of PCC at any visit post-Baseline

End point title	Number of participants with hematology parameters of PCC at any visit post-Baseline
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End point description:

Laboratory samples were collected for analysis of hematology parameters. The PCC values for hematology parameters: hematocrit was 1.02 x Upper limit of normal (ULN), for hemoglobin was 1.03 x ULN, for lymphocytes was 0.81 x lower limit of normal (LLN), for platelet count was 0.67 x LLN and 1.57 x ULN, for total neutrophils was 0.83 x LLN, and that for white blood cell count was 0.67 x LLN and value of 1.82 x ULN. Only those parameters for which a value of PCC was reported at any visit post-Baseline have been presented.

End point type	Secondary
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End point timeframe:

Up to Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61 <sup>[46]</sup>	125 <sup>[47]</sup>		
Units: Participants				
Hematocrit > reference range high	12	27		
Hemoglobin > reference range high	2	6		
Lymphocytes < reference range low	6	9		
Platelet count > reference range high	1	0		
Platelet count < reference range low	0	1		
Total neutrophils < reference range low	8	9		
White blood cell count < reference range low	3	4		

Notes:

[46] - Safety Population

[47] - Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with coagulation parameters of PCC at any visit post-Baseline

End point title	Number of participants with coagulation parameters of PCC at any visit post-Baseline
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End point description:

Laboratory samples were collected for analysis of coagulation parameters. The PCC values for coagulation parameters activated partial thromboplastin time (aPTT) was 1.5 x ULN and aPTT ratio also known as international normalized ratio (INR) was 1.2 x ULN. Only those parameters for which a value of PCC was reported at any visit post-Baseline is presented.

End point type	Secondary
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End point timeframe:

Up to Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61 <sup>[48]</sup>	125 <sup>[49]</sup>		
Units: Participants				
aPTT > reference range high	6	6		
INR > reference range high	11	32		

Notes:

[48] - Safety Population

[49] - Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with clinical chemistry parameters of PCC at any visit post-Baseline

End point title	Number of participants with clinical chemistry parameters of
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## End point description:

Laboratory samples were collected for analysis of chemistry parameters. The PCC values for chemistry parameters for alanine amino transferase (ALT) plus total bilirubin (TB) was  $\geq 1.5 \times \text{ULN}$  for TB and  $\geq 2 \times \text{ULN}$  for ALT, for albumin was  $0.86 \times \text{LLN}$ , for aspartate amino transferase (AST) was  $\geq 2 \times \text{ULN}$ , for calcium was  $0.91 \times \text{LLN}$  and  $1.06 \times \text{ULN}$ , for glucose was  $0.71 \times \text{LLN}$  and  $1.41 \times \text{ULN}$ , for phosphorus was  $0.80 \times \text{LLN}$  and  $1.14 \times \text{ULN}$ , for sodium was  $0.96 \times \text{LLN}$  and  $1.03 \times \text{ULN}$ , for potassium was  $0.86 \times \text{LLN}$  and  $1.10 \times \text{ULN}$  and that for alkaline phosphatase was  $\geq 2 \times \text{ULN}$ . Only those parameters for which a value of PCC was reported at any visit post-Baseline is presented.

End point type	Secondary
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End point timeframe:

Up to Week 48

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61 <sup>[50]</sup>	125 <sup>[51]</sup>		
Units: Participants				
ALT plus TB > reference range high	0	2		
ALT > reference range high	61	125		
Albumin < reference range low	0	1		
AST > reference range high	61	125		
Calcium > reference range high	1	3		
Calcium < reference range low	0	3		
Glucose > reference range high	3	5		
Glucose < reference range low	0	2		
Phosphorus > reference range high	1	8		
Sodium > reference range high	2	9		
Potassium > reference range high	0	0		
Potassium < reference range low	0	0		
Alkaline phosphatase > reference range high	0	0		

Notes:

[50] - Safety Population

[51] - Safety Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of participants with urinalysis data outside the reference range (>reference range high) at any visit post- Baseline**

End point title	Number of participants with urinalysis data outside the reference range (>reference range high) at any visit post-Baseline
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End point description:

Urine samples were collected for analysis of abnormal urine parameters. Quantitative examination included the assessment for urine albumin excretion rate, urine alpha-1-microglobulin, urine creatinine excretion-24 hour and urine protein excretion-24 hour. Only those parameters for which a value of >reference range high was reported at any visit post-Baseline is presented.

End point type	Secondary
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End point timeframe:

Up to Week 48



End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61 <sup>[52]</sup>	125 <sup>[53]</sup>		
Units: Participants				
Urine Albumin excretion rate > reference range	1	15		
Urine Protein excretion-24 hour > reference range	4	54		

Notes:

[52] - Safety Population. Only those participants available at the specified time points were analyzed.

[53] - Safety Population. Only those participants available at the specified time points were analyzed.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Plasma Concentrations of GSK2402968 Following Subcutaneous Administration

End point title	Plasma Concentrations of GSK2402968 Following Subcutaneous Administration
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End point description:

Blood samples for pharmacokinetic assessment were taken at Week 0 (Randomization) at 0.5, 1, 3 hours post-dose and at Week 8,12, 24, 36 and 47 at pre-dose, and between 1 and 4 hours post-dose. Data has been presented for plasma concentrations of GSK2402968 following subcutaneous administration. The pharmacokinetic population comprised all participants who were randomized to the study and from whom at least one blood sample was obtained for assessment of GSK2402968 concentration. Only those participants available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Secondary
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End point timeframe:

Randomization (Week 0 at 0.5, 1 and 3 hours), Week 8 (pre-dose, 1-4 hours), Week 12 (pre-dose, 1-4 hours), Week 24 (pre-dose, 1-4 hours), Week 36 (pre-dose, 1-4 hours), Week 47 (pre-dose, 1-4 hours)

End point values	Placebo	GSK2402968 6mg/kg/week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 <sup>[54]</sup>	125 <sup>[55]</sup>		
Units: Nanograms per millimeter				
median (full range (min-max))				
Week 0, 0.5 hours; n=120	( to )	3349.595 (572.07 to 10408.94)		
Week 0, 1 hour; n=122	( to )	4946.950 (1094.90 to 13159.51)		
Week 0, 3 hour; n=121	( to )	5932.740 (1794.00 to 12765.26)		
Week 8, Pre-dose; n=47	( to )	12.730 (0.00 to 4424.28)		

Week 8, 1-4 hours; n=47	( to )	5100.220 (7.62 to 10471.64)		
Week 12, Pre-dose; n=47	( to )	19.090 (4.60 to 50.95)		
Week 12, 1-4 hours; n=47	( to )	5613.040 (10.89 to 10583.33)		
Week 24, Pre-dose; n=49	( to )	40.920 (0.00 to 186.87)		
Week 24, 1-4 hours; n=49	( to )	6141.580 (40.65 to 11902.15)		
Week 36, Pre-dose; n=38	( to )	55.185 (22.64 to 6590.81)		
Week 36, 1-4 hours; n=37	( to )	5755.950 (68.84 to 12967.56)		
Week 47, Pre-dose; n=106	( to )	61.395 (3.86 to 5922.31)		
Week 47, 1-4 hours; n=99	( to )	5266.240 (46.42 to 13841.11)		

Notes:

[54] - Cannot measure plasma concentrations of verum in the placebo group

[55] - Pharmacokinetic Population

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to Follow-up (Week 68)

Adverse event reporting additional description:

The Safety Population was used for analysis.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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### Reporting groups

Reporting group title	Placebo
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Reporting group description:

Participants received single dose of matching placebo sterile solution for subcutaneous injection preferably in the morning over the 48 week treatment period.

Reporting group title	GSK2402968 6mg/kg/week
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Reporting group description:

Participants received single dose of GSK2402968 6 mg/kg/week subcutaneous injection preferably in the morning over the 48 week treatment period.

Serious adverse events	Placebo	GSK2402968 6mg/kg/week	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 61 (8.20%)	13 / 125 (10.40%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	1 / 61 (1.64%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 61 (1.64%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac fibrillation			
subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			

subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Benign intracranial hypertension			
subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intercostal neuralgia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial venous sinus thrombosis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Spinal pain			
subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Glomerulonephritis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			

subjects affected / exposed	1 / 61 (1.64%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 61 (1.64%)	0 / 125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 61 (0.00%)	1 / 125 (0.80%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	Placebo	GSK2402968 6mg/kg/week	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 61 (95.08%)	123 / 125 (98.40%)	
Investigations			
Protein urine present			
subjects affected / exposed	4 / 61 (6.56%)	17 / 125 (13.60%)	
occurrences (all)	9	30	
Red blood cells urine positive			
subjects affected / exposed	4 / 61 (6.56%)	14 / 125 (11.20%)	
occurrences (all)	5	18	
Cystatin C increased			
subjects affected / exposed	2 / 61 (3.28%)	14 / 125 (11.20%)	
occurrences (all)	4	18	
Red blood cells urine			
subjects affected / exposed	4 / 61 (6.56%)	11 / 125 (8.80%)	
occurrences (all)	6	21	
Urine protein/creatinine ratio increased			
subjects affected / exposed	2 / 61 (3.28%)	11 / 125 (8.80%)	
occurrences (all)	3	18	
Blood fibrinogen decreased			

subjects affected / exposed occurrences (all)	6 / 61 (9.84%) 8	3 / 125 (2.40%) 3	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	12 / 61 (19.67%)	27 / 125 (21.60%)	
occurrences (all)	16	54	
Contusion			
subjects affected / exposed	7 / 61 (11.48%)	8 / 125 (6.40%)	
occurrences (all)	10	19	
Excoriation			
subjects affected / exposed	3 / 61 (4.92%)	7 / 125 (5.60%)	
occurrences (all)	3	9	
Ligament sprain			
subjects affected / exposed	3 / 61 (4.92%)	7 / 125 (5.60%)	
occurrences (all)	4	7	
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 61 (18.03%)	33 / 125 (26.40%)	
occurrences (all)	27	97	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	4 / 61 (6.56%)	62 / 125 (49.60%)	
occurrences (all)	6	494	
Injection site discolouration			
subjects affected / exposed	2 / 61 (3.28%)	41 / 125 (32.80%)	
occurrences (all)	3	230	
Pyrexia			
subjects affected / exposed	15 / 61 (24.59%)	27 / 125 (21.60%)	
occurrences (all)	23	42	
Injection site pain			
subjects affected / exposed	2 / 61 (3.28%)	23 / 125 (18.40%)	
occurrences (all)	3	41	
Injection site reaction			
subjects affected / exposed	1 / 61 (1.64%)	24 / 125 (19.20%)	
occurrences (all)	3	105	
Injection site bruising			

subjects affected / exposed	6 / 61 (9.84%)	11 / 125 (8.80%)	
occurrences (all)	18	168	
Injection site induration			
subjects affected / exposed	0 / 61 (0.00%)	17 / 125 (13.60%)	
occurrences (all)	0	35	
Injection site pruritus			
subjects affected / exposed	0 / 61 (0.00%)	17 / 125 (13.60%)	
occurrences (all)	0	34	
Injection site haematoma			
subjects affected / exposed	2 / 61 (3.28%)	9 / 125 (7.20%)	
occurrences (all)	4	21	
Injection site atrophy			
subjects affected / exposed	0 / 61 (0.00%)	9 / 125 (7.20%)	
occurrences (all)	0	12	
Injection site urticaria			
subjects affected / exposed	0 / 61 (0.00%)	9 / 125 (7.20%)	
occurrences (all)	0	38	
Injection site swelling			
subjects affected / exposed	0 / 61 (0.00%)	8 / 125 (6.40%)	
occurrences (all)	0	20	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	4 / 61 (6.56%)	6 / 125 (4.80%)	
occurrences (all)	5	7	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	13 / 61 (21.31%)	28 / 125 (22.40%)	
occurrences (all)	18	53	
Diarrhoea			
subjects affected / exposed	9 / 61 (14.75%)	23 / 125 (18.40%)	
occurrences (all)	20	38	
Abdominal pain			
subjects affected / exposed	7 / 61 (11.48%)	14 / 125 (11.20%)	
occurrences (all)	11	22	
Abdominal pain upper			



subjects affected / exposed occurrences (all)	3 / 61 (4.92%) 19	9 / 125 (7.20%) 12	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)  Epistaxis subjects affected / exposed occurrences (all)  Oropharyngeal pain subjects affected / exposed occurrences (all)	 12 / 61 (19.67%) 18  5 / 61 (8.20%) 6  1 / 61 (1.64%) 1	 24 / 125 (19.20%) 30  11 / 125 (8.80%) 15  10 / 125 (8.00%) 15	
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)  Erythema subjects affected / exposed occurrences (all)  Pruritus subjects affected / exposed occurrences (all)	 6 / 61 (9.84%) 7  1 / 61 (1.64%) 1  1 / 61 (1.64%) 1	 3 / 125 (2.40%) 3  7 / 125 (5.60%) 40  7 / 125 (5.60%) 8	
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)  Haematuria subjects affected / exposed occurrences (all)	 11 / 61 (18.03%) 18  5 / 61 (8.20%) 11	 42 / 125 (33.60%) 99  21 / 125 (16.80%) 43	
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all)  Back pain subjects affected / exposed occurrences (all)	 12 / 61 (19.67%) 28  5 / 61 (8.20%) 7	 11 / 125 (8.80%) 21  8 / 125 (6.40%) 12	

Arthralgia			
subjects affected / exposed	1 / 61 (1.64%)	10 / 125 (8.00%)	
occurrences (all)	1	12	
Muscle spasms			
subjects affected / exposed	4 / 61 (6.56%)	5 / 125 (4.00%)	
occurrences (all)	6	5	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	25 / 61 (40.98%)	38 / 125 (30.40%)	
occurrences (all)	45	68	
Upper respiratory tract infection			
subjects affected / exposed	8 / 61 (13.11%)	15 / 125 (12.00%)	
occurrences (all)	18	26	
Gastroenteritis			
subjects affected / exposed	6 / 61 (9.84%)	15 / 125 (12.00%)	
occurrences (all)	5	19	
Rhinitis			
subjects affected / exposed	3 / 61 (4.92%)	10 / 125 (8.00%)	
occurrences (all)	5	14	
Influenza			
subjects affected / exposed	4 / 61 (6.56%)	7 / 125 (5.60%)	
occurrences (all)	4	7	
Ear infection			
subjects affected / exposed	5 / 61 (8.20%)	4 / 125 (3.20%)	
occurrences (all)	5	4	
Pharyngitis			
subjects affected / exposed	4 / 61 (6.56%)	5 / 125 (4.00%)	
occurrences (all)	6	5	
Bronchitis			
subjects affected / exposed	4 / 61 (6.56%)	4 / 125 (3.20%)	
occurrences (all)	5	6	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 September 2010	This amendment applied to all sites and countries and: corrected previous errors discovered post finalization of original protocol; added further justification to the selection of 6 mg/kg weekly dosing; added new wording regarding the rotation of injection sites; changed frequency of collection of dystrophin antibodies to reduce the blood volumes; expanded the window for performing muscle biopsy; changed the timing for the 24 hour urine collection timing; clarified wording around the use of concomitant medications; added language clarifying that dual-energy X-ray absorptiometry (DEXA) should not be performed when there may be confounders to interpretation (e.g. on boys with metal rods/metal implants which could create artefacts); added language around stopping and follow-up criteria for laboratory safety parameters related to liver, renal inflammation and disseminated intravascular coagulation (DIC); revised statistical analysis sections; updated the Sponsor Information Page and added additional Quality of Life instrument, the Health Utilities Index (HUI).
21 June 2011	This amendment applied to all countries and all sites and was implemented to update the safety monitoring criteria, to remove the requirement for contraception, added MRI sub-study in Brazil and Argentina, updated the study design and End of Treatment section to allow for subjects who withdraw early from the study for safety reasons to enter the extension study. This allowed subjects for whom the risk:benefit assessment supports continued treatment to have further access to drisapersen. This amendment also implemented the addition of two secondary endpoints as requested by European Medicines Agency (EMA)
31 October 2011	This country/site specific amendment was implemented to comply with local requirements in Italy related to the requirement for contraception
21 June 2012	This amendment updated renal safety monitoring criteria, reporting updates for serious adverse events (SAEs), and added clarification to the DIC criteria. Medical Monitor contact information was also updated as there was a change to the Medical Monitor.

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported