Clinical trial results:
A double-blind, escalating dose, randomized, placebo-controlled study to assess the pharmacokinetics, safety and tolerability of single subcutaneous injections of GSK2402968 in non-ambulant subjects with Duchenne muscular dystrophy

Summary

EudraCT number	2010-024566-22
Trial protocol	FR Outside EU/EEA
Global end of trial date	28 February 2012

Results information

Result version number	v1 (current)
This version publication date	03 August 2019
First version publication date	03 August 2019

Trial information

Trial identification

Sponsor protocol code	DMD114118

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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 Respoonse Centre, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@GSK.com
Scientific contact	GSK Respoonse 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)	EMEA-000746-PIP01-09
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 August 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2012
Global end of trial reached?	Yes
Global end of trial date	28 February 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the pharmacokinetics, safety and tolerability of GSK2402968 after a single subcutaneous administration at different dose levels in non-ambulatory subjects with Duchenne muscular dystrophy.

Protection of trial subjects:

This study was performed in compliance with Good Clinical Practices and GlaxoSmithKline Standard Operating Procedures for all processes involved, including the archiving of essential documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 July 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

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	20
EEA total number of subjects	4

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)	3
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 at 2 study centers in United States and France.

Pre-assignment

Screening details:

A total of 21 subjects were screened and 20 subjects randomized into the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Single dose of placebo sterile solution for subcutaneous injection.

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

Dosage and administration details:

Single dose of placebo sterile solution for subcutaneous injection.

Arm title	3mg/kg GSK2402968

Arm description:

Single dose of 3mg/kg GSK2402968 sterile solution for subcutaneous injection

Arm type	Experimental
Investigational medicinal product name	GSK2402968
Investigational medicinal product code	
Other name	Drisapersen
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single dose of 3mg/kg GSK2402968 sterile solution for subcutaneous injection

Arm title	6mg/kg GSK2402968

Arm description:

Single dose of 6mg/kg GSK2402968 sterile solution for subcutaneous injection

Arm type	Experimental
Investigational medicinal product name	GSK2402968
Investigational medicinal product code	
Other name	Drisapersen
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single dose of 6mg/kg GSK2402968 sterile solution for subcutaneous injection

Arm title	9mg/kg GSK2402968

Arm description:

Single dose of 9mg/kg GSK2402968 sterile solution for subcutaneous injection.

Arm type	Experimental
Investigational medicinal product name	GSK2402968
Investigational medicinal product code	
Other name	Drisapersen
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single dose of 9mg/kg GSK2402968 sterile solution for subcutaneous injection

Number of subjects in period 1	Placebo	3mg/kg GSK2402968	6mg/kg GSK2402968
Started	5	6	6
Completed	5	6	6

Number of subjects in period 1	9mg/kg GSK2402968
Started	3
Completed	3

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Single dose of placebo sterile solution for subcutaneous injection.	
Reporting group title	3mg/kg GSK2402968
Reporting group description:	
Single dose of 3mg/kg GSK2402968 sterile solution for subcutaneous injection	
Reporting group title	6mg/kg GSK2402968
Reporting group description:	
Single dose of 6mg/kg GSK2402968 sterile solution for subcutaneous injection	
Reporting group title	9mg/kg GSK2402968
Reporting group description:	
Single dose of 9mg/kg GSK2402968 sterile solution for subcutaneous injection.	

Reporting group values	Placebo	3mg/kg GSK2402968	6mg/kg GSK2402968
Number of subjects	5	6	6
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	12.2	13.8	13.3
standard deviation	± 0.84	± 1.72	± 1.21
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	5	6	6
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	2	0
Not Hispanic or Latino	4	4	5
Unknown or Not Reported	1	0	1
Race			
Units: Subjects			
White - Arabic/North African Heritage	0	0	2
White - White/Caucasian/European Heritage	4	6	3
Not Reported	1	0	1
Body Mass Index (BMI)			
Units: kg/m^2			
arithmetic mean	23.68	22.73	29.07
standard deviation	± 11.12	± 6.14	± 6.85
Weight			
Units: kg			
arithmetic mean	49.1	50.45	59.08
standard deviation	± 14.00	± 13.52	± 12.09

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Single dose of placebo sterile solution for subcutaneous injection.	
Reporting group title	3mg/kg GSK2402968
Reporting group description:	
Single dose of 3mg/kg GSK2402968 sterile solution for subcutaneous injection	
Reporting group title	6mg/kg GSK2402968
Reporting group description:	
Single dose of 6mg/kg GSK2402968 sterile solution for subcutaneous injection	
Reporting group title	9mg/kg GSK2402968
Reporting group description:	
Single dose of 9mg/kg GSK2402968 sterile solution for subcutaneous injection.	

Primary: Number of Subjects With Treatment Emergent Adverse Ev
Follow-Up Adverse events (AE's)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Follow-Up Adverse events (AE's)[1]

End point description:

Safety Population are all subjects who received a dose of study medication.

Adverse Events (AEs) classified into treatment emergent AEs and follow-up AEs.

Treatment emergent AEs occurring from the start of study treatment up to and including Day 28.

Follow-up AEs are those AEs beginning from Day 29 up to and including the final follow-up contact.

Adverse Events of special interest resulting from any of the Laboratory Safety Parameter Stopping Criteria for hepatic or renal toxicity, thrombocytes, inflammation and coagulation occurring and also any AEs resulting from injection site reactions.

End point type	Primary
End point timeframe:	
Up to 5 months	

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 for safety evaluation.

End point values	Placebo	3mg/kg GSK2402968	6mg/kg GSK2402968	9mg/kg GSK2402968
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	6	3
Units: participants				
Treatment Emergent	2	6	6	3
Follow-up	2	3	4	0
Drug related Adverse Events	1	5	5	3
AE's of Special Interest - Injection Site Reaction	1	4	5	3
AE's of Special Interest - Renal Toxicity	0	0	0	1
AE's of Special Interest - Inflammation	0	0	1	3
Deaths	0	0	0	0

Serious Adverse Events by Phase	0	0	0	0
Adverse Events Leading to Withdrawal	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax) of GSK240

End point title	Maximum Observed Plasma Concentration (Cmax) of GSK2402968[2][3]

End point description:

Pharmacokinetic Parameters Cmax is the observed maximum plasma concentration post-dose.

PK Population subjects in the 'Safety' population for whom a pharmacokinetic sample was obtained and analysed. This population was used for all PK summaries.

End point type	Primary

End point timeframe:

At 0.25, 0.5, 1, 3, 6, 9, 24hrs, Days 4, 8 and 29-35

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: The Statistical Analysis is not the comparision between the doses, it is to Estimate Dose Proportionality after Single Dose.
[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Statistical Analysis is not the comparision between the doses, it is to Estimate Dose Proportionality after Single Dose.

End point values	3mg/kg GSK2402968	6mg/kg GSK2402968	9mg/kg GSK2402968	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	3	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	4990 (± 36.0)	8140 (± 25.9)	8940 (± 20.8)	

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve From Ti Measurable Concentration [AUC(0-t)] of GSK2402968

End point title	Area Under the Plasma Concentration-time Curve From Time 0 to the Last Measurable Concentration [AUC(0-t)] of GSK2402968[4][5]

End point description:

Pharmacokinetic Parameters [AUC(0-t)] is Area under the plasma concentration-time curve from Time 0 to last measured concentration

PK Population subjects

End point type	Primary

End point timeframe:

At 0.25, 0.5, 1, 3, 6, 9, 24hrs, Days 4, 8 and 29-35

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: The Statistical Analysis is not the comparision between the doses, it is to Estimate Dose Proportionality after Single Dose.
[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Statistical Analysis is not the comparision between the doses, it is to Estimate Dose Proportionality after Single Dose.

End point values	3mg/kg GSK2402968	6mg/kg GSK2402968	9mg/kg GSK2402968	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	3	
Units: ng.hr/mL				
geometric mean (geometric coefficient of variation)	48100 (± 15.4)	98800 (± 28.0)	107000 (± 9.1)	

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve From Ti post-dose [AUC(0-24)] of GSK2402968

End point title	Area Under the Plasma Concentration-time Curve From Time 0 to 24 hours post-dose [AUC(0-24)] of GSK2402968[6][7]

End point description:

Pharmacokinetic Parameters [AUC(0-24h)] is the Area under the plasma concentration-time curve from Time 0 to 24 hours post-dose

PK Population subjects

End point type	Primary

End point timeframe:

At 0.25, 0.5, 1, 3, 6, 9, 24hrs, Days 4, 8 and 29-35

Notes:

[6] - 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: The Statistical Analysis is not the comparision between the doses, it is to Estimate Dose Proportionality after Single Dose.
[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Statistical Analysis is not the comparision between the doses, it is to Estimate Dose Proportionality after Single Dose.

End point values	3mg/kg GSK2402968	6mg/kg GSK2402968	9mg/kg GSK2402968	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	3	
Units: ng.hr/mL				
geometric mean (geometric coefficient of variation)	44600 (± 18.5)	87800 (± 33.4)	97800 (± 10.7)	

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve From Ti post-dose [AUC(0-7d)] of GSK2402968

End point title	Area Under the Plasma Concentration-time Curve From Time 0 to 7 days post-dose [AUC(0-7d)] of GSK2402968[8][9]

End point description:

Pharmacokinetic Parameters [AUC(0-7d)] is Area under the plasma concentration-time curve from Time 0 to 7 days post-dose

PK Population subjects

End point type	Primary

End point timeframe:

At 0.25, 0.5, 1, 3, 6, 9, 24hrs, Days 4, 8 and 29-35

Notes:

[8] - 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: The Statistical Analysis is not the comparision between the doses, it is to Estimate Dose Proportionality after Single Dose.
[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Statistical Analysis is not the comparision between the doses, it is to Estimate Dose Proportionality after Single Dose.

End point values	3mg/kg GSK2402968	6mg/kg GSK2402968	9mg/kg GSK2402968	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	3	
Units: ng.hr/mL				
geometric mean (geometric coefficient of variation)	45500 (± 16.0)	87300 (± 18.7)	112000 (± 0.6)	

Statistical analyses

No statistical analyses for this end point

Primary: Time of maximum plasma concentration (tmax) of GSK2402

End point title	Time of maximum plasma concentration (tmax) of GSK2402968[10][11]

End point description:

Pharmacokinetic Parameters (tmax) is the time of maximum plasma concentration post-dose.

PK Population subjects

End point type	Primary

End point timeframe:

At 0.25, 0.5, 1, 3, 6, 9, 24hrs, Days 4, 8 and 29-35

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: The Statistical Analysis is not the comparision between the doses, it is to Estimate Dose Proportionality after Single Dose.
[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Statistical Analysis is not the comparision between the doses, it is to Estimate Dose Proportionality after Single Dose.

End point values	3mg/kg GSK2402968	6mg/kg GSK2402968	9mg/kg GSK2402968	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	3	
Units: hr^2				
median (full range (min-max))	3.01 (2.97 to 5.78)	3.00 (2.98 to 6.00)	6.00 (3.00 to 6.00)	

Statistical analyses

No statistical analyses for this end point

Primary: Apparent plasma clearance (CL/F) of GSK2402968

End point title	Apparent plasma clearance (CL/F) of GSK2402968[12][13]

End point description:

Pharmacokinetic Parameters (CL/F) is the Apparent plasma clearance

PK Population subjects

End point type	Primary

End point timeframe:

At 0.25, 0.5, 1, 3, 6, 9, 24hrs, Days 4, 8 and 29-35

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: The Statistical Analysis is not the comparision between the doses, it is to Estimate Dose Proportionality after Single Dose.
[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Statistical Analysis is not the comparision between the doses, it is to Estimate Dose Proportionality after Single Dose.

End point values	3mg/kg GSK2402968	6mg/kg GSK2402968		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	1		
Units: mL/hr				
arithmetic mean (standard deviation)	3700.6 (± 834.94)	3770.8 (± 0)		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Up to 5 months

Adverse event reporting additional description:

Adverse Events (AEs) for this study were classified into treatment emergent AEs and follow-up AEs.

Treatment emergent AEs were defined as AEs occurring from the start of study treatment up to and including Day 28.
Follow-up AEs were defined as those AEs beginning from Day 29 up to and including the final follow-up contact.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	3mg/kg GSK2402968
Reporting group description: -	
Reporting group title	6mg/kg GSK2402968
Reporting group description: -	
Reporting group title	9mg/kg GSK2402968

Reporting group description: -

Serious adverse events	Placebo	3mg/kg GSK2402968	6mg/kg GSK2402968
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	9mg/kg GSK2402968		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Placebo	3mg/kg GSK2402968	6mg/kg GSK2402968
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	6 / 6 (100.00%)	6 / 6 (100.00%)
Investigations			
Alpha 1 microglobulin increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Immunology test abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	1 / 5 (20.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	1	1	2
General disorders and administration site conditions			
Injection site discolouration			
subjects affected / exposed	1 / 5 (20.00%)	4 / 6 (66.67%)	5 / 6 (83.33%)
occurrences (all)	1	4	8
Injection site erythema			
subjects affected / exposed	0 / 5 (0.00%)	3 / 6 (50.00%)	1 / 6 (16.67%)
occurrences (all)	0	3	1
Injection site haematoma			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	0	1	2
Injection site induration			
subjects affected / exposed	1 / 5 (20.00%)	3 / 6 (50.00%)	4 / 6 (66.67%)
occurrences (all)	1	3	5
Injection site inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Injection site oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Injection site pruritus			
subjects affected / exposed	0 / 5 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Injection site warmth			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Upper respiratory tract congestion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			

subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	3
Bronchitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 5 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	9mg/kg GSK2402968		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Investigations			
Alpha 1 microglobulin increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
C-reactive protein increased			

subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Immunology test abnormal			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
General disorders and administration site conditions			
Injection site discolouration			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	3		
Injection site erythema			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	3		
Injection site haematoma			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Injection site induration			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Injection site inflammation			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	3		
Injection site oedema			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	3		
Injection site pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Injection site pruritus			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%)		

subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Infections and infestations			
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 May 2010	Protocol Amendment 1 was a global amendment for all countries, all centers that was released prior to any screening into the study. The purpose of this amendment was to: 1. Increase the number of subjects from 24 to 32, with 6 active and 2 placebo subjects per cohort 2. Increase time between cohorts to a minimum of 14 days 3. Remove guarantee of a follow-on study 4. Clarify the role of the Independent Data Monitoring Committee (IDMC) 5. Exclusion Criterion #5: Reduce the exclusionary period for idebenone and Coenzyme Q10 to 1 month
12 January 2011	Protocol Amendment 2 was a country specific amendment for France. This amendment was approved after 13 subjects had been randomized and the purpose of this amendment was to: Add Inclusion Criterion #11, a social security entry criterion specific to French subjects
20 April 2011	Protocol Amendment 3 was a global amendment for all countries, all centers. This amendment was approved after 14 subjects had been randomized and the amendment was at the request of the French regulatory authority, Afsaaps, to: Add inflammatory markers as a dose limiting criterion.
20 August 2011	Protocol Amendment 4 was a global amendment for all countries, all centers. This amendment was approved after 18 subjects had been randomized and the purpose of this amendment was to: 1. Update the safety monitoring criteria, following discussions with the FDA, to add Complement Factor C3 and clarify C Reactive Protein (CRP) testing is high sensitivity CRP (hsCRP). This ensured consistency across the GSK2402968 program. 2. Remove Inclusion Criterion #8 regarding contraceptive requirements. Additional data became available which supported removal of need to use contraception.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported