Clinical trial results:
SMT C1100 - A Phase 1, Open-label, Single and Multiple Oral Dose, Safety, Tolerability and Pharmacokinetic Study in Paediatric Patients with Duchenne Muscular Dystrophy

Summary

EudraCT number	2013-002115-99
Trial protocol	GB
Global end of trial date	23 April 2014

Results information

Result version number	v1 (current)
This version publication date	07 July 2016
First version publication date	05 August 2015

Trial information

Trial identification

Sponsor protocol code	SMT C11002

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Summit Corporation plc
Sponsor organisation address	85b Park Drive, Milton Park, Abingdon, Oxfordshire, United Kingdom, OX14 4RY
Public contact	Clinical Trial Information, Summit Corporation plc, dmd@summitplc.com
Scientific contact	Clinical Trial Information, Summit Corporation plc, dmd@summitplc.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 April 2014
Global end of trial reached?	Yes
Global end of trial date	23 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to determine the safety and tolerability of single and multiple oral doses of SMT C1100 in patients with Duchenne Muscular Dystrophy (DMD).

Protection of trial subjects:

Following discussion of the study with study site personnel, the patient's parents/legal guardians signed a study-specific informed consent form in the presence of a study site physician or a suitably trained deputy to indicate that they were freely giving their informed consent. An age-specific informed assent form was reviewed with the patient by the site personnel and the patient's parents/legal guardians. Written or verbal assent of the patient was considered for inclusion and was documented within the patient medical notes.

A safety review was performed following each initial dosing, and there was a 48 hour period between dosing of each patient. In addition, there was at least 2 weeks between each dose escalation, to allow a satisfactory review of safety, tolerability and pharmacokinetics data. The project team led by the Sponsor's Chief Medical Officer and Chief Investigator conducted the safety reviews.

Background therapy:

During the study, systemic corticosteroids (stable dose for 2 months prior to start of study), bisphosphonates, beta blockers, angiotensin-receptor blockers and angiotensin converting enzyme inhibitors were permitted.

Evidence for comparator:

Not applicable; no comparators were used.

Actual start date of recruitment	02 December 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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

Subject disposition

Recruitment

Recruitment details:

The first informed consent was given on 2nd December 2013, and the date of last patient last visit was 23rd April 2014. The final post-study observation was made on 8th May 2014.

Pre-assignment

Screening details:

Screening was performed within 28 days prior to initial dosing.

Pre-assignment period milestones

Number of subjects started	13[1]
Number of subjects completed	12

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen failure according to exclusion criteria: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Thirteen patients were screened for inclusion in the study, however one patient was excluded as a screen failure. Twelve patients were dosed with SMT C1100, and data are reported for these patients.

Period 1

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

Blinding implementation details:

Not applicable.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

Patients in Group A were dosed with SMT C1100 according to the following regimen:

Day 1: 50 mg/kg (single dose at 0 hours)
Days 2 to 10: 50 mg/kg twice daily (at approximately 0 hours and 12 hours)
Day 11: 50 mg/kg (single dose at 0 hours)

Arm type	Experimental
Investigational medicinal product name	SMT C1100
Investigational medicinal product code	SMT C1100
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Aqueous microfluidised suspension of SMT C1100 (200 mg/g) was administered using oral dosing syringes, according to the treatment group regimen.

Arm title	Group B

Arm description:

Following completion of Group A dosing and safety/pharmacokinetics review, patients in Group B were dosed according to the following regimen:

Day 1: 100 mg/kg (single dose at 0 hours)
Days 2 to 10: 100 mg/kg twice daily (at approximately 0 hours and 12 hours)
Day 11: 100 mg/kg (single dose at 0 hours)

Arm type	Experimental
Investigational medicinal product name	SMT C1100
Investigational medicinal product code	SMT C1100
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Aqueous microfluidised suspension of SMT C1100 (200 mg/g) was administered using oral dosing syringes, according to the treatment group regimen.

Arm title	Group C

Arm description:

Following completion of Group B dosing and safety/pharmacokinetics review, patients in Group C were dosed according to the following regimen:

Day 1: 100 mg/kg (single dose at 0 hours)
Days 2 to 10: 100 mg/kg three times daily, with 5 to 7 hours between doses where possible (0 hours, 5 to 7 hours and 10 to 14 hours; after breakfast, lunch and evening meal, respectively)
Day 11: 100 mg/kg (single dose at 0 hours)

Arm type	Experimental
Investigational medicinal product name	SMT C1100
Investigational medicinal product code	SMT C1100
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Aqueous microfluidised suspension of SMT C1100 (200 mg/g) was administered using oral dosing syringes, according to the treatment group regimen.

Number of subjects in period 1	Group A	Group B	Group C
Started	4	4	4
Completed	4	4	4

Baseline characteristics

Reporting groups	
Reporting group title	Group A

Reporting group description:

Patients in Group A were dosed with SMT C1100 according to the following regimen:

Day 1: 50 mg/kg (single dose at 0 hours)
Days 2 to 10: 50 mg/kg twice daily (at approximately 0 hours and 12 hours)
Day 11: 50 mg/kg (single dose at 0 hours)

Reporting group title	Group B

Reporting group description:

Following completion of Group A dosing and safety/pharmacokinetics review, patients in Group B were dosed according to the following regimen:

Day 1: 100 mg/kg (single dose at 0 hours)
Days 2 to 10: 100 mg/kg twice daily (at approximately 0 hours and 12 hours)
Day 11: 100 mg/kg (single dose at 0 hours)

Reporting group title	Group C

Reporting group description:

Following completion of Group B dosing and safety/pharmacokinetics review, patients in Group C were dosed according to the following regimen:

Day 1: 100 mg/kg (single dose at 0 hours)
Days 2 to 10: 100 mg/kg three times daily, with 5 to 7 hours between doses where possible (0 hours, 5 to 7 hours and 10 to 14 hours; after breakfast, lunch and evening meal, respectively)
Day 11: 100 mg/kg (single dose at 0 hours)

Reporting group values	Group A	Group B	Group C
Number of subjects	4	4	4
Age categorical Units: Subjects			
Children (2-11 years)	4	4	4
Age continuous Units: years			
arithmetic mean	9	8	8
full range (min-max)	6 to 11	6 to 8	6 to 10
Gender categorical Units: Subjects			
Female	0	0	0
Male	4	4	4
Age of DMD diagnosis Units: years			
arithmetic mean	5	4	4
full range (min-max)	4 to 8	2 to 6	3 to 5
Time since DMD diagnosis Units: years			
arithmetic mean	4	4	4
full range (min-max)	2 to 5	2 to 6	3 to 5

Reporting group values	Total		
Number of subjects	12		
Age categorical Units: Subjects			
Children (2-11 years)	12		
Age continuous Units: years arithmetic mean full range (min-max)	- -		
Gender categorical Units: Subjects			
Female Male	0 12		
Age of DMD diagnosis Units: years arithmetic mean full range (min-max)	- -		
Time since DMD diagnosis Units: years arithmetic mean full range (min-max)	- -		

End points

End points reporting groups

Reporting group title	Group A

Reporting group description:

Patients in Group A were dosed with SMT C1100 according to the following regimen:

Day 1: 50 mg/kg (single dose at 0 hours)
Days 2 to 10: 50 mg/kg twice daily (at approximately 0 hours and 12 hours)
Day 11: 50 mg/kg (single dose at 0 hours)

Reporting group title	Group B

Reporting group description:

Following completion of Group A dosing and safety/pharmacokinetics review, patients in Group B were dosed according to the following regimen:

Day 1: 100 mg/kg (single dose at 0 hours)
Days 2 to 10: 100 mg/kg twice daily (at approximately 0 hours and 12 hours)
Day 11: 100 mg/kg (single dose at 0 hours)

Reporting group title	Group C

Reporting group description:

Following completion of Group B dosing and safety/pharmacokinetics review, patients in Group C were dosed according to the following regimen:

Day 1: 100 mg/kg (single dose at 0 hours)
Days 2 to 10: 100 mg/kg three times daily, with 5 to 7 hours between doses where possible (0 hours, 5 to 7 hours and 10 to 14 hours; after breakfast, lunch and evening meal, respectively)
Day 11: 100 mg/kg (single dose at 0 hours)

Primary: Safety and tolerability of single and multiple oral doses of SMT C1100

End point title	Safety and tolerability of single and multiple oral doses of SMT C1100[1]

End point description:

The condition of each patient was monitored throughout the study. When resident at the study sites any signs or symptoms were observed and elicited at least once a day by open questioning. Patients were also encouraged to spontaneously report adverse events occurring at any other time during the study by documenting in their diary and/or verbally reporting them to Investigator staff when at the study site.

End point type	Primary

End point timeframe:

Duration of the study.

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: The primary endpoint for this study was assessment of safety and tolerability. Appropriate descriptive statistics for the safety data were determined, but no inferential statistical analyses were performed on safety data.

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: Number of events				
Patients with treatment-emergent adverse events	4	4	3	
Number of treatment-emergent adverse events	15	9	7	
Patients with serious adverse events	0	0	0	
Patients discontinued owing to adverse events	0	0	0	
Patients with severe adverse events	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: AUC 0-tlast SMT C1100

End point title	AUC 0-tlast SMT C1100

End point description:

Area under the plasma concentration versus time curve from time zero up to the last quantifiable concentration (Day 1 only).

End point type	Secondary

End point timeframe:

Day 1 (following single oral dosing).

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)	330 (± 147.5)	547 (± 177.6)	385 (± 107.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: AUC 0-tau SMT C1100

End point title	AUC 0-tau SMT C1100

End point description:

Area under the plasma concentration versus time curve over a dosing interval. The dosing interval tau was 12 hours for twice daily dosing and 6 hours for three times daily dosing regimens.

End point type	Secondary

End point timeframe:

Day 11 (following multiple oral dosing).

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)	128 (± 158.7)	187 (± 247.7)	87.2 (± 130.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax Day 1 SMT C1100

End point title	Cmax Day 1 SMT C1100
End point description:	
Maximum observed plasma concentration.	
End point type	Secondary
End point timeframe:	
Day 1 (following single oral dosing).	

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	77.6 (± 145.6)	145 (± 78.7)	88.5 (± 77.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax Day 11 SMT C1100

End point title	Cmax Day 11 SMT C1100
End point description:	
Maximum observed plasma concentration.	
End point type	Secondary
End point timeframe:	
Day 11 (following multiple oral dosing).	

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	26.7 (± 81.8)	31.1 (± 198)	20.4 (± 147.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: tmax Day 1 SMT C1100

End point title	tmax Day 1 SMT C1100

End point description:

Time of maximum observed plasma concentration.

End point type	Secondary

End point timeframe:

Day 1 (following single oral dosing).

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: hour				
median (full range (min-max))	1.02 (1 to 4.02)	1.58 (1.03 to 2.05)	1 (0.98 to 1)	

Statistical analyses

No statistical analyses for this end point

Secondary: tmax Day 11 SMT C1100

End point title	tmax Day 11 SMT C1100

End point description:

Time of maximum observed plasma concentration.

End point type	Secondary

End point timeframe:

Day 11 (following multiple oral dosing).

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: hour				
median (full range (min-max))	1.51 (1 to 6)	2.01 (1 to 3)	1 (1 to 1)	

Statistical analyses

No statistical analyses for this end point

Secondary: t1/2 Day 1 SMT C1100

End point title	t1/2 Day 1 SMT C1100
End point description: Apparent terminal elimination half life.	
End point type	Secondary
End point timeframe: Day 1 (following single oral dosing).	

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: hour				
arithmetic mean (standard deviation)	6.15 (± 3.07)	4.98 (± 2.21)	9.99 (± 7.55)	

Statistical analyses

No statistical analyses for this end point

Secondary: t1/2 Day 11 SMT C1100

End point title	t1/2 Day 11 SMT C1100
End point description: Apparent terminal elimination half life.	
End point type	Secondary
End point timeframe: Day 11 (following multiple oral dosing).	

End point values	Group A	Group B	Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	4	3	
Units: hour				
arithmetic mean (standard deviation)	7.99 (± 6.42)	6.81 (± 3.83)	6.92 (± 2.64)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The condition of each patient was monitored throughout the study. In addition, when resident at the study sites any signs or symptoms were observed and elicited at least once a day by open questioning.

Adverse event reporting additional description:

Patients were also encouraged to spontaneously report adverse events occurring at any other time during the study by documenting in their diary and/or verbally reporting them to Investigator staff when at the study site. Unique preferred terms for adverse events were only counted once per patient.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Group A

Reporting group description:

Patients in Group A were dosed with SMT C1100 according to the following regimen:

Day 1: 50 mg/kg (single dose at 0 hours)
Days 2 to 10: 50 mg/kg twice daily (at approximately 0 hours and 12 hours)
Day 11: 50 mg/kg (single dose at 0 hours)

Reporting group title	Group B

Reporting group description:

Following completion of Group A dosing and safety/pharmacokinetics review, patients in Group B were dosed according to the following regimen:

Day 1: 100 mg/kg (single dose at 0 hours)
Days 2 to 10: 100 mg/kg twice daily (at approximately 0 hours and 12 hours)
Day 11: 100 mg/kg (single dose at 0 hours)

Reporting group title	Group C

Reporting group description:

Following completion of Group B dosing and safety/pharmacokinetics review, patients in Group C were dosed according to the following regimen:

Day 1: 100 mg/kg (single dose at 0 hours)
Days 2 to 10: 100 mg/kg three times daily, with 5 to 7 hours between doses where possible (0 hours, 5 to 7 hours and 10 to 14 hours; after breakfast, lunch and evening meal, respectively)
Day 11: 100 mg/kg (single dose at 0 hours)

Serious adverse events	Group A	Group B	Group C
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Group A	Group B	Group C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	4 / 4 (100.00%)	3 / 4 (75.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Energy increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Faeces pale			
subjects affected / exposed	1 / 4 (25.00%)	3 / 4 (75.00%)	3 / 4 (75.00%)
occurrences (all)	1	3	3
Diarrhoea			
subjects affected / exposed	2 / 4 (50.00%)	1 / 4 (25.00%)	1 / 4 (25.00%)
occurrences (all)	2	1	1
Abdominal pain upper			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Abdominal pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

Frequent bowel movements			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Sneezing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Rash erythematous			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Mood swings			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Not applicable.

Notes: