



## Clinical trial results:

**SMT C11003 - A Phase 1b placebo-controlled, multi-centre, randomized, double-blind 3-period dose escalation study to evaluate the pharmacokinetics (PK) and safety of SMT C1100 in paediatric patients with Duchenne Muscular Dystrophy (DMD) who follow a balanced diet.**

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

## Summary

EudraCT number	2014-003100-78
Trial protocol	GB
Global end of trial date	06 July 2015

## Results information

Result version number	v1 (current)
This version publication date	17 June 2016
First version publication date	17 June 2016

## Trial information

### Trial identification

Sponsor protocol code	SMT C11003
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### Additional study identifiers

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

Notes:

## Sponsors

Sponsor organisation name	Summit (Oxford) Limited
Sponsor organisation address	85b Park Drive, Milton Park, Abingdon, Oxfordshire, United Kingdom, OX14 4RY
Public contact	Clinical Trial Information, Summit (Oxford) Limited, 44 1235 443939, dmd@summitplc.com
Scientific contact	Clinical Trial Information, Summit (Oxford) Limited, 44 1235 443939, 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	10 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 July 2015
Global end of trial reached?	Yes
Global end of trial date	06 July 2015
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD who follow a balanced diet

Protection of trial subjects:

Prior to commencement of the study, each patient and their parent/legal guardian were provided with a study-specific assent form and informed consent form giving details of the investigational medicinal product, procedures and potential risks involved. For a patient not qualified or incapable of giving legal consent, written consent was obtained from the legally acceptable representative (legal guardian). Informed consent was obtained from the patient's legally acceptable representative (legal guardian) plus the caregiver's assent (if caregiver was other than the legal guardian). The patient's assent was also obtained, consistent with local regulations. Patients and their parent/legal guardian were instructed that they were free to obtain further information from the Investigator and that they were free to withdraw their consent and to discontinue their participation in the study at any time. At the same time, the parent/legal guardian was informed about the existence of an indemnification procedure between the Sponsor and the Investigator and their obligations in this respect.

Background therapy:

During the study, systemic corticosteroids (stable dose for 6 months prior to start of study), angiotensin converting enzyme inhibitors, angiotensin-receptor blockers, beta blockers, bisphosphonates and vitamin D and calcium supplements were permitted.

Evidence for comparator:

Not applicable

Actual start date of recruitment	04 February 2015
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)	10
Adolescents (12-17 years)	2
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 04 February 2015, and the date of the final post study observation was 06 July 2015

### Pre-assignment

Screening details:

Patients were screened no more than 4 weeks prior to their first dose and 3 weeks prior to the dietary run-in period.

### 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	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

Selected members of the Clinical Research Organisation (CRO) Pharmacokinetic (PK) group were unblinded in order to assess PK data from the preceding treatment period to determine whether stopping criteria for SMT C1100 had been met at each dose escalation meeting. The CRO, Sponsor, and Chief Investigator may also have been unblinded to the treatment assignment if a patient met stopping criteria.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Treatment sequence 1

Arm description:

Subjects who received SMT C1100 1250mg twice daily in treatment period 1, placebo twice daily in treatment period 2, and SMT C1100 2500mg twice daily in treatment period 3.

Each patient received a single dose on Day 1, followed by twice-daily dosing on Days 2 to 14 in each treatment period.

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

Dosage and administration details:

On each dosing occasion, patients swallowed 12.4 mL (2 x 6.2 mL doses) of an aqueous microfluidised suspension of SMT C1100 via a dosing syringe, immediately after consuming a healthy balanced meal. Patients were then given 100 mL of milk to swallow immediately following dosing.

Two bottles were used for each dosing, with 6.2 mL drawn from each bottle for each dose. Therefore, when receiving 1250 mg SMT C1100 1 bottle contained SMT C1100 and the other contained placebo; and when receiving 2500 mg SMT C1100 both bottles contained SMT C1100.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

On each dosing occasion, patients swallowed 12.4 mL (2 x 6.2 mL doses) of placebo via a dosing syringe, immediately after consuming a healthy balanced meal. Patients were then given 100 mL of

milk to swallow immediately following dosing.

Two bottles were used for each dosing, with 6.2 mL drawn from each bottle for each dose. Therefore, when receiving placebo both the 2 bottles contained placebo.

<b>Arm title</b>	Treatment sequence 2
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Arm description:

Subjects who received SMT C1100 1250mg twice daily in treatment period 1, SMT C1100 2500mg twice daily in treatment period 2, and placebo twice daily in treatment period 3.

Each patient received a single dose on Day 1, followed by twice-daily dosing on Days 2 to 14 in each treatment period.

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

Dosage and administration details:

On each dosing occasion, patients swallowed 12.4 mL (2 x 6.2 mL doses) of an aqueous microfluidised suspension of SMT C1100 via a dosing syringe, immediately after consuming a healthy balanced meal. Patients were then given 100 mL of milk to swallow immediately following dosing.

Two bottles were used for each dosing, with 6.2 mL drawn from each bottle for each dose. Therefore, when receiving 1250 mg SMT C1100 1 bottle contained SMT C1100 and the other contained placebo; and when receiving 2500 mg SMT C1100 both bottles contained SMT C1100.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

On each dosing occasion, patients swallowed 12.4 mL (2 x 6.2 mL doses) of placebo via a dosing syringe, immediately after consuming a healthy balanced meal. Patients were then given 100 mL of milk to swallow immediately following dosing.

Two bottles were used for each dosing, with 6.2 mL drawn from each bottle for each dose. Therefore, when receiving placebo both the 2 bottles contained placebo.

<b>Arm title</b>	Treatment sequence 3
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Arm description:

Subjects who received placebo twice daily in treatment period 1, SMT C1100 1250mg twice daily in treatment period 2, and SMT C1100 2500mg twice daily in treatment period 3.

Each patient received a single dose on Day 1, followed by twice-daily dosing on Days 2 to 14 in each treatment period.

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

Dosage and administration details:

On each dosing occasion, patients swallowed 12.4 mL (2 x 6.2 mL doses) of an aqueous microfluidised suspension of SMT C1100 via a dosing syringe, immediately after consuming a healthy balanced meal. Patients were then given 100 mL of milk to swallow immediately following dosing.

Two bottles were used for each dosing, with 6.2 mL drawn from each bottle for each dose. Therefore, when receiving 1250 mg SMT C1100 1 bottle contained SMT C1100 and the other contained placebo; and when receiving 2500 mg SMT C1100 both bottles contained SMT C1100.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

**Dosage and administration details:**

On each dosing occasion, patients swallowed 12.4 mL (2 x 6.2 mL doses) of placebo via a dosing syringe, immediately after consuming a healthy balanced meal. Patients were then given 100 mL of milk to swallow immediately following dosing.

Two bottles were used for each dosing, with 6.2 mL drawn from each bottle for each dose. Therefore, when receiving placebo both the 2 bottles contained placebo.

<b>Number of subjects in period 1</b>	Treatment sequence 1	Treatment sequence 2	Treatment sequence 3
Started	4	4	4
Treatment period 1	4	4	4
Treatment period 2	4	4	4
Treatment period 3	4	4	4
Completed study	4	4	4
Completed	4	4	4

## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	12	12	
Age categorical			
Units: Subjects			
5-7 years	4	4	
8-11 years	6	6	
12-13 years	2	2	
Age continuous			
Units: years			
arithmetic mean	9.19		
full range (min-max)	6.6 to 13	-	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	12	12	
Race			
Units: Subjects			
Asian	1	1	
White	11	11	
Age at DMD diagnosis			
Patient age at diagnosis of Duchenne muscular dystrophy			
Units: years			
arithmetic mean	4.3		
full range (min-max)	1.1 to 7.7	-	
Time since DMD diagnosis			
Time since diagnosis of Duchenne muscular dystrophy			
Units: years			
arithmetic mean	4.53		
full range (min-max)	1.3 to 11.9	-	
Weight			
Patient weight			
Units: kg			
arithmetic mean	31.18		
full range (min-max)	20.5 to 49	-	
BMI			
Body Mass Index			
Units: kg/square metre			
arithmetic mean	19.35		
full range (min-max)	14.9 to 26.1	-	
Historical NSAA score			
Historical North Star Ambulatory Assessment score			
Units: Score			
arithmetic mean	23.5		

full range (min-max)	10 to 33	-	
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## End points

### End points reporting groups

Reporting group title	Treatment sequence 1
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Reporting group description:

Subjects who received SMT C1100 1250mg twice daily in treatment period 1, placebo twice daily in treatment period 2, and SMT C1100 2500mg twice daily in treatment period 3.

Each patient received a single dose on Day 1, followed by twice-daily dosing on Days 2 to 14 in each treatment period.

Reporting group title	Treatment sequence 2
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Reporting group description:

Subjects who received SMT C1100 1250mg twice daily in treatment period 1, SMT C1100 2500mg twice daily in treatment period 2, and placebo twice daily in treatment period 3.

Each patient received a single dose on Day 1, followed by twice-daily dosing on Days 2 to 14 in each treatment period.

Reporting group title	Treatment sequence 3
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Reporting group description:

Subjects who received placebo twice daily in treatment period 1, SMT C1100 1250mg twice daily in treatment period 2, and SMT C1100 2500mg twice daily in treatment period 3.

Each patient received a single dose on Day 1, followed by twice-daily dosing on Days 2 to 14 in each treatment period.

Subject analysis set title	SMT C1100 1250mg Day 1
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Subject analysis set type	Full analysis
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Subject analysis set description:

Patients who received a single dose of SMT C1100 at 1250mg on Day 1

Subject analysis set title	SMT C1100 1250mg Day 14
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Subject analysis set type	Full analysis
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Subject analysis set description:

Patients who received a dose of SMT C1100 at 1250mg twice-daily from Day 2 - Day 14

Subject analysis set title	SMT C1100 1250mg Day 14 - AM
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Subject analysis set type	Full analysis
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Subject analysis set description:

Patients who received a dose of SMT C1100 at 1250mg twice-daily from Day 2 - Day 14; data from samples post AM dose on Day 14

Subject analysis set title	SMT C1100 1250mg Day 14 - PM
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Subject analysis set type	Full analysis
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Subject analysis set description:

Patients who received a dose of SMT C1100 at 1250mg twice-daily from Day 2 - Day 14; data from samples post PM dose on Day 14

Subject analysis set title	SMT C1100 2500mg Day 1
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Subject analysis set type	Full analysis
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Subject analysis set description:

Patients who received a single dose of SMT C1100 at 2500mg on Day 1

Subject analysis set title	SMT C1100 2500mg Day 14
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Subject analysis set type	Full analysis
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Subject analysis set description:

Patients who received a dose of SMT C1100 at 2500mg twice-daily from Day 2 - Day 14

Subject analysis set title	SMT C1100 2500mg Day 14 - AM
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Subject analysis set type	Full analysis
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Subject analysis set description:

Patients who received a dose of SMT C1100 at 2500mg twice-daily from Day 2 - Day 14; data from samples post AM dose on Day 14

Subject analysis set title	SMT C1100 2500mg Day 14 - PM
Subject analysis set type	Full analysis
Subject analysis set description:	
Patients who received a dose of SMT C1100 at 2500mg twice-daily from Day 2 - Day 14; data from samples post PM dose on Day 14	

### Primary: AUC 0-infinity (Day 1) - SMT C1100

End point title	AUC 0-infinity (Day 1) - SMT C1100 <sup>[1]</sup>
End point description:	
Area under the plasma concentration-time curve from zero to infinity	
End point type	Primary
End point timeframe:	
PK blood samples taken after dosing on Day 1	

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 objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 1	SMT C1100 2500mg Day 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	9		
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)				
SMT C1100	359 (± 104)	474 (± 107)		

### Statistical analyses

No statistical analyses for this end point

### Primary: AUC 0-infinity (Day 1) - Dihydrodiol I

End point title	AUC 0-infinity (Day 1) - Dihydrodiol I <sup>[2]</sup>
End point description:	
Area under the plasma concentration-time curve from zero to infinity	
End point type	Primary
End point timeframe:	
PK blood samples taken after dosing on Day 1	

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 primary objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 1	SMT C1100 2500mg Day 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	11		
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)				
Dihydrodiol I	5360 (± 42)	6470 (± 47.2)		

## Statistical analyses

No statistical analyses for this end point

### Primary: AUC 0-infinity (Day 1) - Dihydrodiol III

End point title	AUC 0-infinity (Day 1) - Dihydrodiol III <sup>[3]</sup>
End point description:	Area under the plasma concentration-time curve from zero to infinity
End point type	Primary
End point timeframe:	PK blood samples taken after dosing on Day 1
Notes:	<p>[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.</p> <p>Justification: The primary objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.</p>

End point values	SMT C1100 1250mg Day 1	SMT C1100 2500mg Day 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	11		
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)				
Dihydrodiol III	10700 (± 60.6)	12700 (± 61.3)		

## Statistical analyses

No statistical analyses for this end point

### Primary: AUC 0-tlast (Day 1) - SMT C1100

End point title	AUC 0-tlast (Day 1) - SMT C1100 <sup>[4]</sup>
End point description:	Area under the plasma concentration-time curve from time zero to time t, where t is the last time point with a measurable concentration
End point type	Primary
End point timeframe:	PK blood samples taken after dosing on Day 1

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 primary objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 1	SMT C1100 2500mg Day 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)				
SMT C1100	290 (± 95.8)	436 (± 97)		

## Statistical analyses

No statistical analyses for this end point

### Primary: AUC 0-tlast (Day 1) - Dihydrodiol I

End point title	AUC 0-tlast (Day 1) - Dihydrodiol I <sup>[5]</sup>
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End point description:

Area under the plasma concentration-time curve from time zero to time t, where t is the last time point with a measurable concentration

End point type	Primary
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End point timeframe:

PK blood samples taken after dosing on Day 1

Notes:

[5] - 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 objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 1	SMT C1100 2500mg Day 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)				
Dihydrodiol I	5090 (± 38.6)	6490 (± 46.5)		

## Statistical analyses

No statistical analyses for this end point

### Primary: AUC 0-tlast (Day 1) - Dihydrodiol III

End point title	AUC 0-tlast (Day 1) - Dihydrodiol III <sup>[6]</sup>
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End point description:

Area under the plasma concentration-time curve from time zero to time t, where t is the last time point with a measurable concentration

End point type Primary

End point timeframe:

PK blood samples taken after dosing on Day 1

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 primary objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 1	SMT C1100 2500mg Day 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)				
Dihydrodiol III	10700 (± 58.7)	12500 (± 58.3)		

## Statistical analyses

No statistical analyses for this end point

## Primary: AUC 0-tau (Day 14) - SMT C1100

End point title AUC 0-tau (Day 14) - SMT C1100<sup>[7]</sup>

End point description:

Area under the plasma concentration-time curve over a dosing interval (tau). The dosing interval (tau) approximated 12 hours. Due to the unequal dosing interval between AM and PM doses, AUC 0-tau was calculated as the total AUC over the sampling period of AM and PM divided by 2

End point type Primary

End point timeframe:

PK blood samples taken after dosing on Day 14

Notes:

[7] - 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 objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 14	SMT C1100 2500mg Day 14		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	11		
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)				
SMT C1100	273 (± 100)	350 (± 132)		

## Statistical analyses

No statistical analyses for this end point

### Primary: AUC 0-tau (Day 14) - Dihydrodiol I

End point title	AUC 0-tau (Day 14) - Dihydrodiol I <sup>[8]</sup>
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End point description:

Area under the plasma concentration-time curve over a dosing interval (tau). The dosing interval (tau) approximated 12 hours. Due to the unequal dosing interval between AM and PM doses, AUC 0-tau was calculated as the total AUC over the sampling period of AM and PM divided by 2

End point type	Primary
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End point timeframe:

PK blood samples taken after dosing on Day 14

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 primary objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 14	SMT C1100 2500mg Day 14		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	11		
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)				
Dihydrodiol I	4870 (± 37.7)	6140 (± 44)		

## Statistical analyses

No statistical analyses for this end point

### Primary: AUC 0-tau (Day 14) - Dihydrodiol III

End point title	AUC 0-tau (Day 14) - Dihydrodiol III <sup>[9]</sup>
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End point description:

Area under the plasma concentration-time curve over a dosing interval (tau). The dosing interval (tau) approximated 12 hours. Due to the unequal dosing interval between AM and PM doses, AUC 0-tau was calculated as the total AUC over the sampling period of AM and PM divided by 2

End point type	Primary
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End point timeframe:

PK blood samples taken after dosing on Day 14

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The primary objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 14	SMT C1100 2500mg Day 14		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	11		
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)				
Dihydrodiol III	11100 (± 43.4)	13600 (± 58.6)		

## Statistical analyses

No statistical analyses for this end point

## Primary: Cmax - SMT C1100

End point title	Cmax - SMT C1100 <sup>[10]</sup>
End point description:	
Maximum observed plasma concentration	
End point type	Primary
End point timeframe:	
PK blood samples taken after dosing on Day 1 or Day 14	

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 primary objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 1	SMT C1100 1250mg Day 14 - AM	SMT C1100 1250mg Day 14 - PM	SMT C1100 2500mg Day 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	12
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
SMT C1100	49 (± 79.8)	38.7 (± 104)	43.1 (± 94)	65.6 (± 74.3)

End point values	SMT C1100 2500mg Day 14 - AM	SMT C1100 2500mg Day 14 - PM		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	11		
Units: ng/mL				

geometric mean (geometric coefficient of variation)				
SMT C1100	44.9 (± 108)	61.2 (± 119)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Cmax - Dihydrodiol I

End point title	Cmax - Dihydrodiol I <sup>[11]</sup>
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End point description:

Maximum observed plasma concentration

End point type	Primary
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End point timeframe:

PK blood samples taken after dosing on Day 1 or Day 14

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The primary objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 1	SMT C1100 1250mg Day 14 - AM	SMT C1100 1250mg Day 14 - PM	SMT C1100 2500mg Day 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	12
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Dihydrodiol I	692 (± 22.5)	631 (± 30.3)	728 (± 39.1)	840 (± 25.1)

End point values	SMT C1100 2500mg Day 14 - AM	SMT C1100 2500mg Day 14 - PM		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	11		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Dihydrodiol I	738 (± 29.1)	894 (± 35.7)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Cmax -Dihydrodiol III



End point title	Cmax -Dihydrodiol III <sup>[12]</sup>
End point description:	
Maximum observed plasma concentration	
End point type	Primary
End point timeframe:	
PK blood samples taken after dosing on Day 1 or Day 14	

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 primary objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 1	SMT C1100 1250mg Day 14 - AM	SMT C1100 1250mg Day 14 - PM	SMT C1100 2500mg Day 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	12
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Dihydrodiol III	1330 (± 37.5)	1370 (± 36.5)	1550 (± 43.2)	1550 (± 33)

End point values	SMT C1100 2500mg Day 14 - AM	SMT C1100 2500mg Day 14 - PM		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	11		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Dihydrodiol III	1520 (± 37.2)	1840 (± 50.1)		

## Statistical analyses

No statistical analyses for this end point

### Primary: tmax - SMT C1100

End point title	tmax - SMT C1100 <sup>[13]</sup>
End point description:	
Time of maximum observed plasma concentration	
End point type	Primary
End point timeframe:	
PK blood samples taken after dosing on Day 1 or Day 14	

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The primary objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 1	SMT C1100 1250mg Day 14 - AM	SMT C1100 1250mg Day 14 - PM	SMT C1100 2500mg Day 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	12
Units: hours				
median (full range (min-max))				
SMT C1100	2.5 (0.98 to 4.1)	4 (2.47 to 6.02)	1.77 (0.5 to 12)	2.5 (1 to 6)

End point values	SMT C1100 2500mg Day 14 - AM	SMT C1100 2500mg Day 14 - PM		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	11		
Units: hours				
median (full range (min-max))				
SMT C1100	4 (2.47 to 10)	2.6 (0.5 to 6.05)		

## Statistical analyses

No statistical analyses for this end point

## Primary: tmax - Dihydrodiol I

End point title tmax - Dihydrodiol I<sup>[14]</sup>

End point description:

Time of maximum observed plasma concentration

End point type Primary

End point timeframe:

PK blood samples taken after dosing on Day 1 or Day 14

Notes:

[14] - 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 objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 1	SMT C1100 1250mg Day 14 - AM	SMT C1100 1250mg Day 14 - PM	SMT C1100 2500mg Day 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	12
Units: hours				
median (full range (min-max))				
Dihydrodiol I	2.53 (1 to 4.1)	3.33 (1.02 to 6.02)	3.27 (1 to 12)	2.56 (1 to 6)

End point values	SMT C1100 2500mg Day 14 - AM	SMT C1100 2500mg Day 14 - PM		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	11		
Units: hours				
median (full range (min-max))				
Dihydrodiol I	4 (2.47 to 6.02)	4 (1 to 6.05)		

## Statistical analyses

No statistical analyses for this end point

## Primary: tmax - Dihydrodiol III

End point title	tmax - Dihydrodiol III <sup>[15]</sup>
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End point description:

Time of maximum observed plasma concentration

End point type	Primary
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End point timeframe:

PK blood samples taken after dosing on Day 1 or Day 14

Notes:

[15] - 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 objective of this study was to determine the single and multiple oral dose PK of SMT C1100 and its metabolites in patients with DMD. Descriptive statistics for the PK data are reported here.

End point values	SMT C1100 1250mg Day 1	SMT C1100 1250mg Day 14 - AM	SMT C1100 1250mg Day 14 - PM	SMT C1100 2500mg Day 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	12
Units: hours				
median (full range (min-max))				
Dihydrodiol III	4 (2.48 to 6.05)	4.03 (2.5 to 6.02)	5 (2.5 to 12)	3.99 (2.5 to 6)

End point values	SMT C1100 2500mg Day 14 - AM	SMT C1100 2500mg Day 14 - PM		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	11		
Units: hours				
median (full range (min-max))				
Dihydrodiol III	4.05 (0 to 9.57)	4 (0.5 to 9)		

## Statistical analyses

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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:

Treatment-Emergent Adverse Events (all causalities) are presented in this record.

Any adverse events and remedial actions required were recorded. The nature, time of onset, duration and severity were documented, together with an Investigator's opinion of the relationship to drug administration.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

### Reporting groups

Reporting group title	SMT C1100 1250mg
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Reporting group description:

Patients who received SMT C1100 at a dose of 1250mg

Reporting group title	SMT C1100 2500mg
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Reporting group description:

Patients who received SMT C1100 at a dose of 2500mg

Reporting group title	SMT C1100 Overall
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Reporting group description:

Patients who received SMT C1100

Reporting group title	Placebo
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Reporting group description:

Patients who received placebo

Serious adverse events	SMT C1100 1250mg	SMT C1100 2500mg	SMT C1100 Overall
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

<b>Non-serious adverse events</b>	SMT C1100 1250mg	SMT C1100 2500mg	SMT C1100 Overall
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	12 / 12 (100.00%)	12 / 12 (100.00%)
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Injury, poisoning and procedural complications			
Injury			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Ligament sprain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Upper limb fracture			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	2	0	2
Lethargy			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Post-traumatic headache			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Sinus headache			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1

Asthenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Faeces pale			
subjects affected / exposed	12 / 12 (100.00%)	11 / 12 (91.67%)	12 / 12 (100.00%)
occurrences (all)	12	12	24
Diarrhoea			
subjects affected / exposed	3 / 12 (25.00%)	3 / 12 (25.00%)	5 / 12 (41.67%)
occurrences (all)	3	3	6
Abdominal pain upper			
subjects affected / exposed	3 / 12 (25.00%)	1 / 12 (8.33%)	3 / 12 (25.00%)
occurrences (all)	5	2	7
Nausea			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	2	0	2
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Haematochezia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	2
Abdominal discomfort			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Constipation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Toothache			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Abdominal pain			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	3	0	3
Cough			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Miliaria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 12 (8.33%)	3 / 12 (25.00%)	3 / 12 (25.00%)
occurrences (all)	2	3	5
Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	1	1	2
Musculoskeletal discomfort			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Rhabdomyolysis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	4 / 12 (33.33%)	2 / 12 (16.67%)	5 / 12 (41.67%)
occurrences (all)	4	2	6



Nail bed infection subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1
Rhinitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1	1 / 12 (8.33%) 1

<b>Non-serious adverse events</b>	Placebo		
Total subjects affected by non-serious adverse events subjects affected / exposed	12 / 12 (100.00%)		
Investigations Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Injury, poisoning and procedural complications Injury subjects affected / exposed occurrences (all)  Ligament sprain subjects affected / exposed occurrences (all)  Upper limb fracture subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0  0 / 12 (0.00%) 0  0 / 12 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all)  Lethargy subjects affected / exposed occurrences (all)  Post-traumatic headache	2 / 12 (16.67%) 2  0 / 12 (0.00%) 0		

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Sinus headache			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
Faeces pale			
subjects affected / exposed	9 / 12 (75.00%)		
occurrences (all)	9		
Diarrhoea			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	5		
Nausea			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Haematochezia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Abdominal discomfort			

<p>subjects affected / exposed</p> <p>0 / 12 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>			
<p>Constipation</p> <p>subjects affected / exposed</p> <p>0 / 12 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>			
<p>Toothache</p> <p>subjects affected / exposed</p> <p>0 / 12 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>			
<p>Abdominal pain</p> <p>subjects affected / exposed</p> <p>1 / 12 (8.33%)</p> <p>occurrences (all)</p> <p>1</p>			
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Rhinorrhoea</p> <p>subjects affected / exposed</p> <p>1 / 12 (8.33%)</p> <p>occurrences (all)</p> <p>1</p> <p>Oropharyngeal pain</p> <p>subjects affected / exposed</p> <p>0 / 12 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>0 / 12 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>			
<p>Skin and subcutaneous tissue disorders</p> <p>Dermatitis allergic</p> <p>subjects affected / exposed</p> <p>0 / 12 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Miliaria</p> <p>subjects affected / exposed</p> <p>1 / 12 (8.33%)</p> <p>occurrences (all)</p> <p>1</p>			
<p>Musculoskeletal and connective tissue disorders</p> <p>Pain in extremity</p> <p>subjects affected / exposed</p> <p>2 / 12 (16.67%)</p> <p>occurrences (all)</p> <p>2</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>0 / 12 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Musculoskeletal discomfort</p>			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Rhabdomyolysis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Nail bed infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported