



## Clinical trial results:

### Arimoclomol prospective double blind, randomised, placebo-controlled study in patients diagnosed with Niemann Pick disease type C

#### Summary

EudraCT number	2015-004438-93
Trial protocol	DK DE IT PL ES GB
Global end of trial date	31 October 2024

#### Results information

Result version number	v1 (current)
This version publication date	20 July 2025
First version publication date	20 July 2025

#### Trial information

##### Trial identification

Sponsor protocol code	CT-ORZY-NPC-002
-----------------------	-----------------

##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02612129
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 124547

Notes:

#### Sponsors

Sponsor organisation name	Zevra Denmark A/S
Sponsor organisation address	Nordre Fasanvej 215, Frederiksberg, Denmark, DK-2000
Public contact	Medical Affairs, Zevra Denmark A/S, 1 8882895607, medicalaffairs@zevra.com
Scientific contact	Medical Affairs, Zevra Denmark A/S, 1 8882895607, medicalaffairs@zevra.com

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001748-PIP01-15
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 April 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2024
Global end of trial reached?	Yes
Global end of trial date	31 October 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

MAIN STUDY: To evaluate therapeutic response to arimoclomol versus placebo, both in addition to best available standard of care, at 12 months.

PEDIATRIC SUB-STUDY: To evaluate the safety and tolerability of arimoclomol in patients aged 6 to <24 months at study enrolment, over 36 months.

OPEN LABEL EXTENSION: To evaluate the long-term therapeutic response (clinical and biological assessments) at 18, 24, 30, 36, 42, 48, 54 and 60 months (after randomization into the double-blind phase of the trial), and to evaluate the safety of arimoclomol.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

All study subjects were required to read and sign an Informed Consent Form.

Background therapy:

Arimoclomol is administered as an add-on therapy to the patient's current prescribed best standard of care; each patient's standard of care may, or may not, include miglustat.

Evidence for comparator: -

Actual start date of recruitment	14 June 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	48 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Switzerland: 2
Worldwide total number of subjects	55
EEA total number of subjects	37

Notes:

<b>Subjects enrolled per age group</b>	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	5
Children (2-11 years)	27
Adolescents (12-17 years)	18
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The main study was conducted at 14 sites and the open label extension study was conducted at 15 sites in the following countries: Denmark, France, Germany, Italy, Poland, Spain, Switzerland, United Kingdom, and United States.

The pediatric substudy was conducted at 4 sites in Denmark, Germany, United Kingdom, and United States.

### Pre-assignment

Screening details:

The Investigator carried out the screening and enrolment for each patient; eligibility criteria was checked for compliance prior to enrolment. To confirm the selected dose in the main study, participants less than 12 years of age underwent an arimoclomol single-dose PK evaluation before randomization and the start of continuous treatment

### Period 1

Period 1 title	Main Study
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

All participants enrolled into the pediatric substudy received open-label arimoclomol.

All participants randomized into the double-blind period were randomized to receive blinded placebo or arimoclomol (with an allocation ratio of 2:1). Both the participants and the investigators were blinded to the treatment assignment and remained blinded throughout the 12-month blinded treatment phase until the final database lock.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Arimoclomol (12-month Double-blind Phase)

Arm description:

Participants received arimoclomol capsules, orally based on participant's body weight, TID for 12 months.

Arm type	Experimental
Investigational medicinal product name	Arimoclomol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Participants received arimoclomol capsules orally three times a day (TID) for 12 months. The dose was 31-124 mg arimoclomol base TID (equivalent to 50-200 mg arimoclomol citrate TID), based on participant's body weight.

<b>Arm title</b>	Placebo (12-month Double-blind Phase)
------------------	---------------------------------------

Arm description:

Participants received matching placebo to arimoclomol capsules, orally based on participant's body weight, TID for 12 months.

Arm type	Placebo
----------	---------

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Participants received matching placebo capsules (with regard to weight, appearance, smell, flavor etc.) orally TID for 12 months.

<b>Arm title</b>	Arimoclomol (36-month pediatric substudy)
------------------	---

Arm description:

Participants received arimoclomol orally based on participant's age and body weight, TID for 36 months.

Arm type	Experimental
Investigational medicinal product name	Arimoclomol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Participants received arimoclomol orally three times a day (TID) for 36 months. The dose was based on participant's age and body weight.

Number of subjects in period 1	Arimoclomol (12-month Double-blind Phase)	Placebo (12-month Double-blind Phase)	Arimoclomol (36-month pediatric substudy)
Started	34	16	5
Completed through 12 months	27	15	4
Completed	27	15	2
Not completed	7	1	3
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	1	-	-
Safety reasons	3	-	-
IMP stopping criteria met	-	1	1
Informed consent withdrawn by LAR	-	-	2
Early escape	2	-	-

## Period 2

Period 2 title	Open-Label Extension Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

## Arms

<b>Arm title</b>	Experimental: Arimoclomol
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Arimoclomol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

**Dosage and administration details:**

Participants received arimoclomol capsules orally three times a day (TID) for 12 months. The dose was 31-124 mg arimoclomol base TID (equivalent to 50-200 mg arimoclomol citrate TID), based on participant's body weight.

<b>Number of subjects in period 2<sup>[1]</sup></b>	Experimental: Arimoclomol
Started	41
Completed	29
Not completed	12
Adverse event, serious fatal	2
Physician decision	2
Safety issues	2
Consent withdrawn by parent/guardian	6

**Notes:**

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: A total of 42 participants completed the double-blind phase, 1 of whom withdrew consent before being dosed in the OLE phase. The remaining 41 participants who completed the double-blind phase were enrolled in the OLE phase. The participants in the pediatric substudy were not eligible to enroll into the OLE phase and therefore do not contribute to the number of participants starting the period.

## Baseline characteristics

### Reporting groups

Reporting group title	Arimoclomol (12-month Double-blind Phase)
Reporting group description:	
Participants received arimoclomol capsules, orally based on participant's body weight, TID for 12 months.	
Reporting group title	Placebo (12-month Double-blind Phase)
Reporting group description:	
Participants received matching placebo to arimoclomol capsules, orally based on participant's body weight, TID for 12 months.	
Reporting group title	Arimoclomol (36-month pediatric substudy)
Reporting group description:	
Participants received arimoclomol orally based on participant's age and body weight, TID for 36 months.	

Reporting group values	Arimoclomol (12-month Double-blind Phase)	Placebo (12-month Double-blind Phase)	Arimoclomol (36-month pediatric substudy)
Number of subjects	34	16	5
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	5
Children (2-11 years)	16	11	0
Adolescents (12-17 years)	13	5	0
Adults (18-64 years)	5	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	17	9	3
Male	17	7	2

Reporting group values	Total		
Number of subjects	55		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	5		
Children (2-11 years)	27		
Adolescents (12-17 years)	18		
Adults (18-64 years)	5		
From 65-84 years	0		
85 years and over	0		

Gender categorical			
Units: Subjects			
Female	29		
Male	26		

### Subject analysis sets

Subject analysis set title	Open-label Arimoclomol (48-month OLE Phase)
Subject analysis set type	Full analysis

Subject analysis set description:

Includes all participants who completed the 12-month double-blind, randomized, placebo-controlled phase of the trial, were eligible for and agreed to participate in the OLE, and subsequently received at least 1 dose of open-label arimoclomol.

Subject analysis set title	Arimoclomol (36-month pediatric substudy)
Subject analysis set type	Safety analysis

Subject analysis set description:

test

Subject analysis set title	Arimoclomol (12-month Double-blind Phase)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received arimoclomol capsules, orally based on participant's body weight, TID for 12 months. Participants formed the Full Analysis Set (FAS), which included participants who were randomized and who received at least one dose of randomized treatment medication (excluding single dose of arimoclomol [patients less than 12 years of age] for the assessment of PK prior to initiation of their randomized treatment).

Subject analysis set title	Placebo (12-month Double-blind Phase)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received matching placebo to arimoclomol capsules, orally based on participant's body weight, TID for 12 months. Participants formed the Full Analysis Set (FAS), which included participants who were randomized and who received at least one dose of randomized treatment medication (excluding single dose of arimoclomol [patients less than 12 years of age] for the assessment of PK prior to initiation of their randomized treatment).

Reporting group values	Open-label Arimoclomol (48-month OLE Phase)	Arimoclomol (36-month pediatric substudy)	Arimoclomol (12-month Double-blind Phase)
Number of subjects	41	5	34
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	5	0
Children (2-11 years)	22	0	16
Adolescents (12-17 years)	16	0	13
Adults (18-64 years)	3	0	5
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	21	3	17
Male	20	2	17



<b>Reporting group values</b>	Placebo (12-month Double-blind Phase)		
Number of subjects	16		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	11		
Adolescents (12-17 years)	5		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Gender categorical Units: Subjects			
Female	9		
Male	7		

## End points

### End points reporting groups

Reporting group title	Arimoclomol (12-month Double-blind Phase)
Reporting group description: Participants received arimoclomol capsules, orally based on participant's body weight, TID for 12 months.	
Reporting group title	Placebo (12-month Double-blind Phase)
Reporting group description: Participants received matching placebo to arimoclomol capsules, orally based on participant's body weight, TID for 12 months.	
Reporting group title	Arimoclomol (36-month pediatric substudy)
Reporting group description: Participants received arimoclomol orally based on participant's age and body weight, TID for 36 months.	
Reporting group title	Experimental: Arimoclomol
Reporting group description: -	
Subject analysis set title	Open-label Arimoclomol (48-month OLE Phase)
Subject analysis set type	Full analysis
Subject analysis set description: Includes all participants who completed the 12-month double-blind, randomized, placebo-controlled phase of the trial, were eligible for and agreed to participate in the OLE, and subsequently received at least 1 dose of open-label arimoclomol.	
Subject analysis set title	Arimoclomol (36-month pediatric substudy)
Subject analysis set type	Safety analysis
Subject analysis set description: test	
Subject analysis set title	Arimoclomol (12-month Double-blind Phase)
Subject analysis set type	Full analysis
Subject analysis set description: Participants received arimoclomol capsules, orally based on participant's body weight, TID for 12 months. Participants formed the Full Analysis Set (FAS), which included participants who were randomized and who received at least one dose of randomized treatment medication (excluding single dose of arimoclomol [patients less than 12 years of age] for the assessment of PK prior to initiation of their randomized treatment).	
Subject analysis set title	Placebo (12-month Double-blind Phase)
Subject analysis set type	Full analysis
Subject analysis set description: Participants received matching placebo to arimoclomol capsules, orally based on participant's body weight, TID for 12 months. Participants formed the Full Analysis Set (FAS), which included participants who were randomized and who received at least one dose of randomized treatment medication (excluding single dose of arimoclomol [patients less than 12 years of age] for the assessment of PK prior to initiation of their randomized treatment).	

### Primary: 1. Change From Baseline in the Niemann-Pick Disease Type C (NPC) Disease Severity Assessed Based on the 5-domain NPCCSS Total Score

End point title	1. Change From Baseline in the Niemann-Pick Disease Type C (NPC) Disease Severity Assessed Based on the 5-domain NPCCSS Total Score
-----------------	---

#### End point description:

NPC disease severity was assessed based on the 5-domain NPC Clinical Severity Scale (NPCCSS). The 5-domain NPCCSS focuses on domains identified by participants, caregivers, and NPC experts as the most clinically relevant when assessing disease progression in NPC: Ambulation, fine motor skills, swallow, cognition, and speech. The scale is derived from the original 17-domain NPCCSS. Each domain is rated on a scale of 0-5 based on clinical assessments, observations, and interviews with participants/caregiver. The total score is a sum of the score of each of the 5 domains and ranges from 0-25, with a higher score indicating more severe clinical impairment.

The analysis is based on the Full Analysis Set (FAS). Overall Number analyzed is the number of participants evaluated at a specified timepoint.

End point type	Primary
End point timeframe:	
Baseline to Month 12	

End point values	Arimoclomol (12-month Double-blind Phase)	Placebo (12-month Double-blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	16		
Units: Score on a scale				
arithmetic mean (standard deviation)	0.7 ( $\pm$ 1.9)	2.0 ( $\pm$ 3.0)		

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
----------------------------	------------------------

Statistical analysis description:

A general linear mixed model (GLMM) for repeated measurements was used for the analysis of NPC disease severity assessed based on the 5-domain NPCCSS scores at Month 12. The general linear mixed model analysis for repeated measures was fitted with treatment, miglustat level and visit as fixed effects including treatment-by-visit interaction and baseline score as a covariate.

Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0456
Method	GLMM for Repeated Measures
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.76
upper limit	-0.03

## Secondary: 2. Percentage of Responders in Clinical Global Impression Scale of Improvement (CGI-I)

End point title	2. Percentage of Responders in Clinical Global Impression Scale of Improvement (CGI-I)
-----------------	--

End point description:

The CGI-I is a 7-point scale that rates total improvement of participant's condition. The clinician rates the participants from 1=Very much improved, 2=Much improved, 3=Minimally improved, 4=No change, 5=Minimally worse, 6=Much worse, or 7=Very much worse. Scores thus range from 1-7 with lower scores indicating greater improvement. Responders were defined as the participants who remained

stable or showed improvement at Month 12.

The analysis is based on the Full Analysis Set (FAS).

End point type	Secondary
End point timeframe:	
Month 12	

End point values	Arimoclomol (12-month Double-blind Phase)	Placebo (12-month Double-blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	16		
Units: Percentage of responders				
number (not applicable)	58.8	56.3		

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Chi-squared Test	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority <sup>[1]</sup>
P-value	= 1
Method	Chi-squared

Notes:

[1] - Participants who discontinued before 12 months have been imputed as non-responders.

## Secondary: 3. Percentage of Responders in 5-domain NPCCSS

End point title	3. Percentage of Responders in 5-domain NPCCSS
-----------------	--

End point description:

The 5-domain NPCCSS focuses on domains identified by participants, caregivers, and NPC experts as the most clinically relevant when assessing disease progression in NPC: Ambulation, fine motor skills, swallow, cognition, and speech. The scale is derived from the original 17-domain NPCCSS. Each domain is rated on a scale of 0-5 based on clinical assessments, observations, and interviews with participants/caregiver. The total score is a sum of the score of each of the 5 domains and ranges from 0-25, with a higher score indicating more severe clinical impairment.

Responders were defined as participants who remained stable or improved compared to baseline. Stable was defined as a participant's total score for the 5 domains being the same at month 12 as at baseline. Improvement was defined as a participant's total score for the 5 domains at month 12 being lower than at baseline.

The analysis is based on the Full Analysis Set (FAS).

End point type	Secondary
End point timeframe:	
Baseline to Month 12	

End point values	Arimoclomol (12-month Double-blind Phase)	Placebo (12-month Double-blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	16		
Units: Percentage of participants				
number (not applicable)	50.0	37.5		

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Fisher's exact test	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority <sup>[2]</sup>
P-value	= 0.5456
Method	Fisher exact

Notes:

[2] - Participants who discontinued before 12 months have been imputed as non-responders.

## Secondary: 4. Time to Worsening

End point title	4. Time to Worsening
End point description: Time to worsening was defined as the time until the participant reached the predefined minimal clinically important difference (MCID) of 2 points compared to baseline on the 5-domain NPC Clinical Severity Scale (NPCCSS). The 5-domain NPCCSS focuses on domains identified by participants, caregivers, and NPC experts as the most clinically relevant when assessing disease progression in NPC: Ambulation, fine motor skills, swallow, cognition, and speech. The scale is derived from the original 17-domain NPCCSS. Each domain is rated on a scale of 0-5 based on clinical assessments, observations, and interviews with participants/caregiver. The total score is a sum of the score of each of the 5 domains and ranges from 0-25, with a higher score indicating more severe clinical impairment.  The values reported per group are the 25th percentile Kaplan-Meier estimates and 95% confidence intervals.  The analysis is based on the Full Analysis Set (FAS).	
End point type	Secondary
End point timeframe: Baseline to Month 12	

End point values	Arimoclomol (12-month Double-blind Phase)	Placebo (12-month Double-blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	16		
Units: Months				
number (confidence interval 95%)	5.2 (2.9 to 12.0)	5.5 (1.0 to 6.5)		

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Log-rank test stratified by miglustat use	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8021
Method	Logrank

## Secondary: 5. Percentage of Participants with Worsening

End point title	5. Percentage of Participants with Worsening
End point description: Worsening was defined as participants that have reached the predefined MCID of 2 points on their 5-domain NPC Clinical Severity Scale (NPCCSS). The 5-domain NPCCSS focuses on domains identified by participants, caregivers, and NPC experts as the most clinically relevant when assessing disease progression in NPC: Ambulation, fine motor skills, swallow, cognition, and speech. The scale is derived from the original 17-domain NPCCSS. Each domain is rated on a scale of 0-5 based on clinical assessments, observations, and interviews with participants/caregiver. The total score is a sum of the score of each of the 5 domains and ranges from 0-25, with a higher score indicating more severe clinical impairment.  Discontinuation before 6 or 12 months was considered as worsened. Missing scores at 6 or 12 months was also considered as worsened.  The analysis is based on the Full Analysis Set (FAS).	
End point type	Secondary
End point timeframe: Months 6 and 12	

End point values	Arimoclomol (12-month Double-blind Phase)	Placebo (12-month Double-blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	16		
Units: Percentage of participants				
number (not applicable)				
Worsening at Month 6	35.3	50.0		
Worsening at Month 12	44.1	43.8		

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Fisher's Exact Test	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority <sup>[3]</sup>
P-value	= 0.3662
Method	Fisher exact

Notes:

[3] - Percentage of participants worsening at Month 6

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Fisher's Exact Test	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority <sup>[4]</sup>
P-value	= 1
Method	Fisher exact

Notes:

[4] - Percentage of participants worsening at Month 12

## Secondary: 6. Change from Baseline in 17-domain NPCCSS Apart from Hearing Domains (i.e. Hearing and Auditory Brainstem Response)

End point title	6. Change from Baseline in 17-domain NPCCSS Apart from Hearing Domains (i.e. Hearing and Auditory Brainstem Response)
-----------------	---

End point description:

The NPC Clinical Severity Scale (NPCCSS) is a disease-specific, clinician-reported outcome measure developed to characterize and quantify NPC disease progression. The 17-domain NPCCSS includes clinical signs and symptoms in nine major and eight minor domains, which are rated on scales of 0-5 (for the major domains) or 0-2 (for the minor domains). The total score is the sum of the score of each of the 17 domains and ranges from 0 to 61, with a high score indicating a more severe clinical impairment.

The analysis is based on the Full Analysis Set (FAS).

End point type	Secondary
End point timeframe:	
Baseline to 6 and 12 months	

End point values	Arimoclomol (12-month Double-blind Phase)	Placebo (12-month Double-blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	16		
Units: Score on a scale				
least squares mean (confidence interval 95%)				
Change at Month 6	0.53 (-0.85 to 1.90)	2.22 (0.33 to 4.10)		
Change at Month 12	1.20 (-0.40 to 2.79)	2.81 (0.75 to 4.87)		

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Change From Baseline in 17-Domain NPCCSS Apart from Hearing Domains (i.e. Hearing and Auditory Brainstem Response) at Month 6 was analyzed using the Analysis of covariance (ANCOVA) model. ANCOVA model was fitted with treatment, baseline full-scale NPCCSS apart from hearing domains score, and use of miglustat as covariates.	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1546
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.04
upper limit	0.66

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Change From Baseline in 17-Domain NPCCSS Apart from Hearing Domains (i.e. Hearing and Auditory Brainstem Response) at Month 12 was analyzed using the ANCOVA model. ANCOVA model was fitted with treatment, baseline full-scale NPCCSS apart from hearing domains score, and use of miglustat as covariates.	



Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2199
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.24
upper limit	1.01

## Secondary: 7. Change from Baseline in 5-domain NPCCSS Score

End point title	7. Change from Baseline in 5-domain NPCCSS Score
End point description:	
The 5-domain NPC Clinical Severity Scale (NPCCSS) focuses on domains identified by participants, caregivers, and NPC experts as the most clinically relevant when assessing disease progression in NPC: Ambulation, fine motor skills, swallow, cognition, and speech. The scale is derived from the original 17-domain NPCCSS. Each domain is rated on a scale of 0-5 based on clinical assessments, observations, and interviews with participants/caregiver. The total score is a sum of the score of each of the 5 domains and ranges from 0-25, with a higher score indicating more severe clinical impairment.	
The analysis is based on the Full Analysis Set (FAS).	
End point type	Secondary
End point timeframe:	
Baseline to 6 months	

End point values	Arimoclomol (12-month Double-blind Phase)	Placebo (12-month Double-blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	16		
Units: Score on a scale				
least squares mean (confidence interval 95%)	0.48 (-0.05 to 1.02)	1.60 (0.86 to 2.34)		

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
An ANCOVA model was fitted with treatment, baseline 5-domain NPCCSS score, and use of miglustat as covariates.	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)

Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0188
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	-1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.03
upper limit	-0.19

## Secondary: 8. Changes from Baseline in Each Individual Domain of the NPCCSS

End point title	8. Changes from Baseline in Each Individual Domain of the NPCCSS
-----------------	--

End point description:

The NPC Clinical Severity Scale (NPCCSS) is a disease-specific, clinician-reported outcome measure developed to characterize and quantify disease progression. The 17-domain NPCCSS includes clinical signs and symptoms in nine major (ambulation, cognition, eye movement, fine motor, hearing, memory, seizures, speech, swallowing,) and eight minor (auditory brainstem response, behavior, gelastic cataplexy, hyperreflexia, incontinence, narcolepsy, psychiatric, respiratory problems) domains, which are rated on scales of 0-5 (for the major domains) or 0-2 (for the minor domains). A higher score indicates a more severe clinical impairment.

The analysis is based on the Full Analysis Set (FAS).

End point type	Secondary
End point timeframe:	
Baseline to 6 and 12 Months	

End point values	Arimoclomol (12-month Double-blind Phase)	Placebo (12- month Double- blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	16		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Ambulation: Baseline	2.5 (± 1.6)	2.2 (± 1.6)		
Ambulation: Change at Month 6	0.1 (± 0.4)	0.3 (± 1.0)		
Ambulation: Change at Month 12	0.3 (± 0.5)	0.3 (± 0.9)		
Speech: Baseline	2.2 (± 1.6)	1.6 (± 1.2)		
Speech: Change at Month 6	0.1 (± 0.5)	0.1 (± 0.3)		
Speech: Change at Month 12	-0.2 (± 1.0)	0.3 (± 0.8)		
Swallow: Baseline	1.9 (± 1.7)	1.3 (± 1.7)		
Swallow: Change at Month 6	0.1 (± 1.1)	0.4 (± 1.0)		
Swallow: Change at Month 12	0.1 (± 1.1)	0.6 (± 1.0)		
Fine Motor Skills: Baseline	2.8 (± 1.8)	1.9 (± 1.8)		
Fine Motor Skills: Change at Month 6	0.1 (± 0.7)	0.5 (± 1.1)		
Fine Motor Skills: Change at Month 12	0.2 (± 0.8)	0.6 (± 1.3)		

Cognition: Baseline	2.8 (± 1.3)	2.5 (± 1.5)		
Cognition: Change at Month 6	0.2 (± 0.5)	0.3 (± 0.8)		
Cognition: Change at Month 12	0.3 (± 0.6)	0.1 (± 0.6)		
Eye Movement: Baseline	2.2 (± 1.2)	2.1 (± 1.1)		
Eye Movement: Change at Month 6	0.0 (± 0.6)	-0.1 (± 0.7)		
Eye Movement: Change at Month 12	0.2 (± 0.9)	-0.1 (± 0.6)		
Memory: Baseline	1.9 (± 1.4)	1.3 (± 1.5)		
Memory: Change at Month 6	0.1 (± 0.5)	0.2 (± 1.1)		
Memory: Change at Month 12	0.1 (± 0.5)	0.3 (± 0.8)		
Seizures: Baseline	1.9 (± 1.9)	1.3 (± 1.8)		
Seizures: Change at Month 6	-0.1 (± 0.8)	0.0 (± 1.5)		
Seizures: Change at Month 12	0.3 (± 0.8)	-0.1 (± 1.7)		
Hearing: Baseline	0.4 (± 1.0)	0.0 (± 0.0)		
Hearing: Change at Month 6	-0.2 (± 0.8)	0.0 (± 0.0)		
Hearing: Change at Month 12	0.0 (± 0.0)	0.3 (± 0.8)		
Auditory Brainstem Response: Baseline	0.2 (± 0.4)	0.1 (± 0.4)		
Auditory Brainstem Response: Change at Month 6	0.0 (± 0.0)	0.2 (± 0.4)		
Auditory Brainstem Response: Change at Month 12	0.0 (± 0.0)	0.0 (± 0.0)		
Behavior: Baseline	0.4 (± 0.6)	0.4 (± 0.6)		
Behavior: Change at Month 6	0.0 (± 0.5)	-0.1 (± 0.5)		
Behavior: Change at Month 12	0.1 (± 0.6)	-0.2 (± 0.4)		
Gelastic Cataplexy: Baseline	0.8 (± 0.9)	0.4 (± 0.8)		
Gelastic Cataplexy: Change at Month 6	0.1 (± 0.5)	0.3 (± 0.6)		
Gelastic Cataplexy: Change at Month 12	0.2 (± 0.6)	0.3 (± 0.6)		
Hyperreflexia: Baseline	1.0 (± 0.7)	1.1 (± 0.9)		
Hyperreflexia: Change at Month 6	-0.0 (± 0.5)	0.2 (± 0.6)		
Hyperreflexia: Change at Month 12	0.1 (± 0.7)	0.1 (± 0.5)		
Incontinence: Baseline	1.0 (± 0.8)	0.8 (± 0.9)		
Incontinence: Change at Month 6	-0.1 (± 0.4)	0.1 (± 0.5)		
Incontinence: Change at Month 12	-0.0 (± 0.4)	0.1 (± 0.9)		
Narcolepsy (NARCO): Baseline	0.1 (± 0.4)	0.3 (± 0.7)		
Narcolepsy (NARCO): Change at Month 6	0.0 (± 0.4)	-0.1 (± 0.3)		
Narcolepsy (NARCO): Change at Month 12	-0.1 (± 0.4)	-0.1 (± 0.3)		
Psychiatric: Baseline	0.1 (± 0.4)	0.1 (± 0.5)		
Psychiatric: Change at Month 6	-0.0 (± 0.3)	0.1 (± 0.6)		
Psychiatric: Change at Month 12	0.0 (± 0.3)	0.0 (± 0.4)		
Respiratory: Baseline	0.1 (± 0.3)	0.0 (± 0.0)		
Respiratory: Change at Month 6	0.0 (± 0.5)	0.1 (± 0.3)		
Respiratory: Change at Month 12	0.1 (± 0.5)	0.2 (± 0.4)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: 9. Change from Baseline in the NPC Clinical Database (NPC-CDB) Score (Modified "Stampfer Score")

End point title	9. Change from Baseline in the NPC Clinical Database (NPC-
-----------------	--

## End point description:

The NPC Clinical Database (NPC-cdb) score aims to reflect the current clinical status of the participant. The NPC-cdb score represents both historical symptoms and a current status. The test consists of ten areas: visceral signs, development, motor function, ocular-motor abnormalities, seizures/cataplexy/narcolepsy, cognitive abilities and memory, behavioral and psychiatric abnormalities, speech, hearing, and abilities in daily life. The current status score is a severity-weighted sum of 72 symptoms considered as disease-relevant at the time of assessment. Each symptom contributes with a score between 1 and 5, the maximum score is 125. An increase in score reflects a reduction in the participant's abilities.

The analysis is based on the Full Analysis Set (FAS).

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline to 6 and 12 Months

End point values	Arimoclomol (12-month Double-blind Phase)	Placebo (12-month Double-blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	16		
Units: Score on a scale				
least squares mean (confidence interval 95%)				
Change at Month 6	-0.38 (-3.30 to 2.54)	4.71 (0.49 to 8.93)		
Change at Month 12	1.85 (-2.16 to 5.86)	4.88 (-0.63 to 10.39)		

## Statistical analyses

Statistical analysis title	Statistical Analysis 1
----------------------------	------------------------

## Statistical analysis description:

Change from baseline in the NPC-CDB score (modified "Stampfer Score") at Month 6 was analyzed using the ANCOVA model. ANCOVA model was fitted with treatment, baseline NPC-CDB total score and use of miglustat as covariates.

Comparison groups	Placebo (12-month Double-blind Phase) v Arimoclomol (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0536
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-5.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.26
upper limit	0.08

<b>Statistical analysis title</b>	Statistical Analysis 2
Statistical analysis description: Change from baseline in the NPC-CDB score (modified "Stampfer Score") at Month 12 was analyzed using the ANCOVA model. ANCOVA model was fitted with treatment, baseline NPC-CDB total score and use of miglustat as covariates.	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3785
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.9
upper limit	3.85

## Secondary: 10. Percentage of Participants with Change from Baseline in Quality of Life (EQ-5D-Y)

End point title	10. Percentage of Participants with Change from Baseline in Quality of Life (EQ-5D-Y)
-----------------	---

End point description:

The EQ-5D-Y descriptive system includes 5 descriptive items: Mobility, self-care, doing usual activities, having pain or discomfort, and feeling anxiety or depressed. Each dimension has 3 levels: No problems, some problems, and a lot of problems. The change in the 5 individual items of the EQ-5D-Y per participant was explored by using the pareto principle at 6 and 12 months to show the number (%) of participants who felt:

- Better (better on at least one dimension and no worse in any other dimension),
- Worse (worse in at least one dimension, and no better in any other dimension)

The analysis is based on the Full Analysis Set (FAS).

End point type	Secondary
End point timeframe: Baseline to 6 and 12 months	

<b>End point values</b>	Arimoclomol (12-month Double-blind Phase)	Placebo (12-month Double-blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	15		
Units: Percentage of participants				
number (not applicable)				

Better: Change at Month 6	16.7	26.7		
Worse: Change at Month 6	40.0	46.7		
Better: Change at Month 12	25.9	40.0		
Worse: Change at Month 12	44.4	20.0		

## Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis 1
Statistical analysis description: Percentage of participants with change from baseline at Month 6 in Quality of Life (EQ-5D-Y) being 'Better', analyzed using a Chi-squared Test	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6951
Method	Chi-squared

<b>Statistical analysis title</b>	Statistical Analysis 2
Statistical analysis description: Percentage of participants with change from baseline at Month 6 in Quality of Life (EQ-5D-Y) being 'Worse', analyzed using a Chi-squared Test	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7542
Method	Chi-squared

<b>Statistical analysis title</b>	Statistical Analysis 3
Statistical analysis description: Percentage of participants with change from baseline at Month 12 in Quality of Life (EQ-5D-Y) being 'Better', analyzed using a Chi-squared Test	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.488
Method	Chi-squared

<b>Statistical analysis title</b>	Statistical Analysis 4
Statistical analysis description: Percentage of participants with change from baseline at Month 12 in Quality of Life (EQ-5D-Y) being 'Worse', analyzed using a Chi-squared Test	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1804
Method	Chi-squared

## Secondary: 11. Change from Baseline in the Scale for Assessment and Rating of Ataxia (SARA) Score

End point title	11. Change from Baseline in the Scale for Assessment and Rating of Ataxia (SARA) Score
-----------------	--

End point description:

The SARA included eight items reflecting neurologic manifestations of cerebellar ataxia. The test provides a direct and simple description of motor function in a participant. The test consists of 8 test items: gait, stance, sitting, speech disturbance, finger chase, nose-finger test, fast alternating hand movements, and heel-shin slide. The total score of the 8 items ranges from 0 (normal cerebellar function) to 40 (not able to perform any of the test items).

The analysis is based on the Full Analysis Set (FAS).

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline to 6 and 12 months

End point values	Arimoclomol (12-month Double-blind Phase)	Placebo (12-month Double-blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	16		
Units: Score on a scale				
least squares mean (confidence interval 95%)				
Change at 6 Months	0.79 (-0.16 to 1.75)	0.05 (-1.29 to 1.40)		
Change at 12 Months	1.06 (-0.17 to 2.29)	0.78 (-0.90 to 2.47)		

## Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis 1
Statistical analysis description: Change from baseline in the SARA score at Month 6 was measured using an ANCOVA model. ANCOVA model was fitted with treatment, baseline SARA score, and use of miglustat as covariates.	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-

	month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.371
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	2.4

<b>Statistical analysis title</b>	Statistical Analysis 2
Statistical analysis description:	
Change from baseline in the SARA score at Month 12 was measured using an ANCOVA model. ANCOVA model was fitted with treatment, baseline SARA score, and use of miglustat as covariates.	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7899
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.82
upper limit	2.37

<b>Secondary: 12. Change from Baseline in the Time Spent to Complete the Nine-Hole Peg Test (9HPT)</b>	
End point title	12. Change from Baseline in the Time Spent to Complete the Nine-Hole Peg Test (9HPT)
End point description:	
The 9HPT test is a direct and simple measurement of fine motor coordination function, eye/hand coordination, and the ability to follow a simple direction. The 9HPT is a timed test in which nine pegs are inserted and removed from nine holes in the pegboard. Both hands are tested starting with the dominant hand. The time spent in completing the 9 HPT using each hand was recorded.	
The analysis is based on the Full Analysis Set (FAS).	
End point type	Secondary
End point timeframe:	
Baseline to 6 and 12 months	



<b>End point values</b>	Arimoclomol (12-month Double-blind Phase)	Placebo (12-month Double-blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	34	16		
Units: Seconds				
least squares mean (confidence interval 95%)				
Dominant Hand: Change at 6 months	1.54 (-24.98 to 28.06)	11.88 (-20.88 to 44.64)		
Non-dominant Hand: Change at 6 months	0.60 (-27.25 to 28.45)	16.46 (-17.07 to 50.00)		
Dominant Hand: Change at 12 months	-3.29 (-15.56 to 8.98)	-6.49 (-20.34 to 7.37)		
Non-dominant Hand: Change at 12 months	11.68 (-14.89 to 38.25)	17.59 (-13.24 to 48.42)		

## Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis 1
Statistical analysis description:	
Dominant Hand: Change From Baseline in the Nine-Hole Peg Test (9HPT) at Month 6 was measured using an ANCOVA model: ANCOVA models were fitted with treatment, baseline dominant/non-dominant hand 9HPT time (secs), and use of miglustat as covariates	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6195
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-10.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53.01
upper limit	32.33

<b>Statistical analysis title</b>	Statistical Analysis 2
Statistical analysis description:	
Non-dominant Hand: Change From Baseline in the Nine-Hole Peg Test (9HPT) at Month 6 was measured using an ANCOVA model: ANCOVA models were fitted with treatment, baseline dominant/non-dominant hand 9HPT time (secs), and use of miglustat as covariates	
Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)

Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4693
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-15.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-60.73
upper limit	29

<b>Statistical analysis title</b>	Statistical Analysis 3
-----------------------------------	------------------------

Statistical analysis description:

Dominant Hand: Change From Baseline in the Nine-Hole Peg Test (9HPT) at Month 12 was measured using an ANCOVA model: ANCOVA models were fitted with treatment, baseline dominant/non-dominant hand 9HPT time (secs), and use of miglustat as covariates

Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7283
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.71
upper limit	22.12

<b>Statistical analysis title</b>	Statistical Analysis 4
-----------------------------------	------------------------

Statistical analysis description:

Non-dominant Hand: Change From Baseline in the Nine-Hole Peg Test (9HPT) at Month 12 was measured using an ANCOVA model: ANCOVA models were fitted with treatment, baseline dominant/non-dominant hand 9HPT time (secs), and use of miglustat as covariates

Comparison groups	Arimoclomol (12-month Double-blind Phase) v Placebo (12-month Double-blind Phase)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7708
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-5.91

Confidence interval	
level	95 %
sides	2-sided
lower limit	-47.54
upper limit	35.72

### Secondary: 13. Percentage of Participants Within Each Severity Category of the Clinical Global Impression Scale of Severity (CGI-S)

End point title	13. Percentage of Participants Within Each Severity Category of the Clinical Global Impression Scale of Severity (CGI-S)
-----------------	--

End point description:

The CGI-S is a 7-point scale that requires the clinician to rate the severity of the participant's illness at the time of assessment. A rating of 1 is considered normal, or with the least severe symptoms, a rating of 7 is extremely ill, or the worst symptoms. Scores thus range from 1-7 with lower scores indicating less severe disease.

The analysis is based on the Full Analysis Set (FAS).

End point type	Secondary
End point timeframe:	
Months 6 and 12	

End point values	Arimoclomol (12-month Double-blind Phase)	Placebo (12- month Double- blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	15		
Units: Percentage of participants				
number (not applicable)				
Month 6: Normal, not ill at all	0	0		
Month 6: Borderline ill	10.3	14.3		
Month 6: Mildly ill	27.6	28.6		
Month 6: Moderately ill	10.3	35.7		
Month 6: Markedly ill	31.0	0		
Month 6: Severely ill	20.7	14.3		
Month 6: Most extremely ill participants	0	7.1		
Month 12: Normal, not ill at all	0	0		
Month 12: Borderline ill	7.4	6.7		
Month 12: Mildly ill	29.6	26.7		
Month 12: Moderately ill	11.1	33.3		
Month 12: Markedly ill	29.6	6.7		
Month 12: Severely ill	22.2	26.7		
Month 12: Most extremely ill participants	0	0		

### Statistical analyses

No statistical analyses for this end point

## Secondary: 14. Percentage of Participants Within Each Category of the Clinical Global Impression Scale of Improvement (CGI-I)

End point title	14. Percentage of Participants Within Each Category of the Clinical Global Impression Scale of Improvement (CGI-I)
-----------------	--

End point description:

The CGI-I is a 7-point scale that rates total improvement of participant's condition. The clinician rates the participants from 1=Very much improved, 2=Much improved, 3=Minimally improved, 4=No change, 5=Minimally worse, 6=Much worse, or 7=Very much worse. Scores thus range from 1-7 with lower scores indicating greater improvement.

The analysis is based on the Full Analysis Set (FAS).

End point type	Secondary
----------------	-----------

End point timeframe:

Months 6 and 12

End point values	Arimoclomol (12-month Double-blind Phase)	Placebo (12- month Double- blind Phase)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	15		
Units: Percentage of participants				
number (not applicable)				
Month 6: Very Much Improved	3.4	0		
Month 6: Much Improved	0	0		
Month 6: Minimally Improved	24.1	25.0		
Month 6: No Change	37.9	25.0		
Month 6: Minimally Worse	27.6	33.3		
Month 6: Much Worse	6.9	16.7		
Month 6: Very Much Worse	0	0		
Month 12: Very Much Improved	0	0		
Month 12: Much Improved	3.7	6.7		
Month 12: Minimally Improved	18.5	33.3		
Month 12: No Change	51.9	20.0		
Month 12: Minimally Worse	14.8	13.3		
Month 12: Much Worse	7.4	26.7		
Month 12: Very Much Worse	3.7	0		

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: 15. Change from OLE Baseline in 5 Domain NPCSS score

End point title	15. Change from OLE Baseline in 5 Domain NPCSS score
-----------------	--

End point description:

NPC disease severity was assessed based on the 5-domain NPC Clinical Severity Scale (NPCCSS). The 5 domain NPCCSS focuses on domains identified by participants, caregivers, and NPC experts as the most

clinically relevant when assessing disease progression in NPC: Ambulation, fine motor skills, swallow, cognition, and speech. The scale is derived from the original 17-domain NPCCSS. Each domain is rated on a scale of 0-5 based on clinical assessments, observations, and interviews with participants/caregiver. The total score is a sum of the score of each of the 5 domains and ranges from 0-25, with a higher score indicating more severe clinical impairment.

End point type	Other pre-specified
End point timeframe:	
OLE Baseline to Month 60	

<b>End point values</b>	Open-label Arimoclomol (48-month OLE Phase)			
Subject group type	Subject analysis set			
Number of subjects analysed	41			
Units: Score on a scale				
arithmetic mean (standard deviation)				
OLE Baseline	12.3 (± 7.8)			
Change from OLE Baseline to Month 18	0.9 (± 1.8)			
Change from OLE Baseline to Month 24	1.1 (± 2.8)			
Change from OLE Baseline to Month 30	1.4 (± 3.1)			
Change from OLE Baseline to Month 36	2.2 (± 4.0)			
Change from OLE Baseline to Month 42	2.0 (± 4.1)			
Change from OLE Baseline to Month 48	2.2 (± 4.3)			
Change from OLE Baseline to Month 54	2.3 (± 4.0)			
Change from OLE Baseline to Month 60	3.2 (± 4.8)			
Change from OLE Baseline to Final OLE visit	2.9 (± 4.7)			

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

In the period following the single dose of arimoclomol (single PK dose), from first to last dose of blinded study drug (12-month Double-Blind Phase) and from first to last dose of open-label study drug (48-month OLE Phase, 36-month pediatric substudy)

Adverse event reporting additional description:

AEs are reported separately for the single dose period where participants received a single dose of arimoclomol, for the 12-month continuous dose period where participants received blinded treatment (arimoclomol or placebo), and for the 48-month OLE period/36-month pediatric substudy where participants received open-label arimoclomol.

Assessment type	Systematic
-----------------	------------

### Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

### Reporting groups

Reporting group title	Arimoclomol Single PK Dose
-----------------------	----------------------------

Reporting group description:

Participants less than 12 years received a single oral dose of arimoclomol capsule, based on participant's body weight, on Day 1.

Reporting group title	Arimoclomol (12-month Double-Blind Phase)
-----------------------	---

Reporting group description:

Participants received arimoclomol capsules, orally based on participant's body weight, TID for 12 months.

Reporting group title	Placebo (12-month Double-blind Phase)
-----------------------	---------------------------------------

Reporting group description:

Participants received matching placebo to arimoclomol capsules, orally based on participant's body weight, TID for 12 months.

Reporting group title	Open-label Arimoclomol (48-month OLE Phase)
-----------------------	---

Reporting group description:

All participants who completed the 12-month double-blind, randomized, placebo-controlled phase of the trial, were eligible for and agreed to participate in the OLE, and subsequently received at least 1 dose of open-label arimoclomol.

Reporting group title	Open-label Arimoclomol (36-month pediatric substudy)
-----------------------	--

Reporting group description:

Participants received open-label arimoclomol, orally based on participant's age and body weight, TID for 36 months.

Serious adverse events	Arimoclomol Single PK Dose	Arimoclomol (12-month Double-Blind Phase)	Placebo (12-month Double-blind Phase)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 28 (7.14%)	5 / 34 (14.71%)	6 / 16 (37.50%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Surgical and medical procedures			
Complete oral rehabilitation			

subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complication associated with device			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory Distress			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic respiratory failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar hypertrophy			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lung consolidation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device leakage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspiration Bronchial			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oxygen saturation decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Craniocerebral Injury			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			



subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patella fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardio-respiratory Arrest			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epileptic Encephalopathy			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 28 (3.57%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dystonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 28 (0.00%)	2 / 34 (5.88%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Foot Deformity			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 34 (0.00%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Tract Infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			

subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Metabolism and nutrition disorders</b>			
<b>Hypophagia</b>			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Malnutrition</b>			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Decreased appetite</b>			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Feeding intolerance</b>			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Dehydration</b>			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Hypoglycaemia</b>			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Open-label Arimoclomol (48- month OLE Phase)	Open-label Arimoclomol (36- month pediatric substudy)	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 41 (36.59%)	2 / 5 (40.00%)	
number of deaths (all causes)	2	0	

number of deaths resulting from adverse events	2	0	
Surgical and medical procedures			
Complete oral rehabilitation			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complication associated with device			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory Distress			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic respiratory failure			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar hypertrophy			

subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung consolidation			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device leakage			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Aspiration Bronchial			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oxygen saturation decreased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Craniocerebral Injury			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Femoral neck fracture			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardio-respiratory Arrest			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epileptic Encephalopathy			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dystonia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	



Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth haemorrhage			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			

subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Foot Deformity			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 41 (7.32%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Tract Infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastroenteritis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 41 (2.44%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			

subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypophagia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Feeding intolerance			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	<b>Arimoclomol Single PK Dose</b>	<b>Arimoclomol (12-month Double-Blind Phase)</b>	<b>Placebo (12-month Double-blind Phase)</b>
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 28 (14.29%)	30 / 34 (88.24%)	13 / 16 (81.25%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Haemangioma of liver subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Vascular disorders Haematoma subjects affected / exposed occurrences (all)  Haemorrhage subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0  0 / 28 (0.00%) 0	1 / 34 (2.94%) 1  0 / 34 (0.00%) 0	0 / 16 (0.00%) 0  0 / 16 (0.00%) 0
Surgical and medical procedures Gastrostomy subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 1	0 / 16 (0.00%) 0
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)  Medical device site reaction subjects affected / exposed occurrences (all)  Fatigue subjects affected / exposed occurrences (all)  Malaise subjects affected / exposed occurrences (all)  Abasia subjects affected / exposed occurrences (all)  Gait disturbance	1 / 28 (3.57%) 1  0 / 28 (0.00%) 0  0 / 28 (0.00%) 0  0 / 28 (0.00%) 0  0 / 28 (0.00%) 0  0 / 28 (0.00%) 0	6 / 34 (17.65%) 15  0 / 34 (0.00%) 0  2 / 34 (5.88%) 2  0 / 34 (0.00%) 0  0 / 34 (0.00%) 0	3 / 16 (18.75%) 4  0 / 16 (0.00%) 0  0 / 16 (0.00%) 0  0 / 16 (0.00%) 0  0 / 16 (0.00%) 0

subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Local swelling			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Medical device site haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Medical device site ulcer			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Unevaluable event			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Medical Device Site Dermatitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Peripheral Swelling			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Secretion Discharge			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Disease progression			

subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Temperature regulation disorder subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Immune system disorders			
Renal abscess subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Seasonal allergy subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	3 / 34 (8.82%) 4	1 / 16 (6.25%) 1
Drug Hypersensitivity subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	1 / 34 (2.94%) 1	0 / 16 (0.00%) 0
Food Allergy subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 1	0 / 16 (0.00%) 0
Social circumstances			
Convalescent subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Reproductive system and breast disorders			
Dysmenorrhoea subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Perineal rash subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Premenstrual Syndrome subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 1	0 / 16 (0.00%) 0
Menstruation irregular subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 1	0 / 16 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Epistaxis			
subjects affected / exposed	0 / 28 (0.00%)	2 / 34 (5.88%)	1 / 16 (6.25%)
occurrences (all)	0	6	1
Oropharyngeal pain			
subjects affected / exposed	0 / 28 (0.00%)	3 / 34 (8.82%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Asthma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Interstitial lung disease			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Aspiration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Bronchial hyperreactivity			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Increased upper airway secretion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Lung disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pneumonia aspiration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory tract inflammation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0



Bronchospasm			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dysphonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nasal Congestion			
subjects affected / exposed	0 / 28 (0.00%)	2 / 34 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Productive Cough			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Illusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Initial insomnia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Aggression			
subjects affected / exposed	0 / 28 (0.00%)	2 / 34 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Agitation			

subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 1	0 / 16 (0.00%) 0
Hallucination, auditory subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 1	0 / 16 (0.00%) 0
Hallucination, visual subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 1	0 / 16 (0.00%) 0
Investigations			
Weight decreased subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	5 / 34 (14.71%) 6	0 / 16 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Blood triglycerides increased subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Blood creatine increased subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 1	0 / 16 (0.00%) 0
Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Blood magnesium increased subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Eosinophil count increased			

subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastric pH decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vitamin D decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Body Temperature Abnormal			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Body Temperature Increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	11	0
C-reactive Protein Increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood iron decreased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Ultrasound liver abnormal			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Laceration			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Expired product administered			

subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 28 (0.00%)	2 / 34 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Stoma site hypergranulation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye contusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye injury			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Lip injury			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Traumatic haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eschar			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Head Injury			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Injury			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Ligament Sprain			

subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	1 / 16 (6.25%) 1
Tooth Injury subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	1 / 16 (6.25%) 1
Congenital, familial and genetic disorders Phimosi subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 1	0 / 16 (0.00%) 0
Nervous system disorders Epilepsy subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 1	2 / 16 (12.50%) 2
Seizure subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	3 / 34 (8.82%) 3	1 / 16 (6.25%) 1
Headache subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	3 / 34 (8.82%) 11	1 / 16 (6.25%) 7
Cataplexy subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Dystonia subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Lethargy subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	2 / 34 (5.88%) 2	0 / 16 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	3 / 34 (8.82%) 3	0 / 16 (0.00%) 0
Generalised tonic-clonic seizure subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Dizziness			

subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Quadriparesis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Ageusia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Coordination abnormal			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Drooling			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dysmetria			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypertonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypotonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Motor dysfunction			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Muscle spasticity			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Neurological decompensation			

subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Partial seizures			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Peripheral sensorimotor neuropathy			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Quadriplegia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Speech disorder			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Tonic convulsion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Cognitive Disorder			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Memory Impairment			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			

subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Peroneal Nerve Palsy			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Petit Mal Epilepsy			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Splenomegaly			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Excessive cerumen production			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Deafness Neurosensory			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Deafness Unilateral			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Ear Pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Middle ear effusion			



subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Corneal epithelium defect			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Corneal opacity			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Saccadic eye movement			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pupils Unequal			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Diplopia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 28 (0.00%)	7 / 34 (20.59%)	2 / 16 (12.50%)
occurrences (all)	0	23	3
Vomiting			
subjects affected / exposed	0 / 28 (0.00%)	8 / 34 (23.53%)	4 / 16 (25.00%)
occurrences (all)	0	26	5
Constipation			
subjects affected / exposed	0 / 28 (0.00%)	7 / 34 (20.59%)	3 / 16 (18.75%)
occurrences (all)	0	14	3
Dysphagia			

subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Anal fissure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Anal haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Inflammatory bowel disease			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Inguinal hernia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Salivary hypersecretion			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Abdominal Pain Upper			
subjects affected / exposed	1 / 28 (3.57%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Abdominal Discomfort			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Aphthous Ulcer			

subjects affected / exposed	0 / 28 (0.00%)	2 / 34 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Dental Caries			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Lip Dry			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Mouth Cyst			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Odynophagia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Tongue ulceration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Anorectal disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hepatic Lesion			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hepatomegaly			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Acne			

subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Acanthosis nigricans			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Angiokeratoma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blister			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dermatitis diaper			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 28 (3.57%)	1 / 34 (2.94%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin lesion			

subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Umbilical discharge			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Angioedema			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dandruff			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Henoch-Schonlein Purpura			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oliguria			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Precocious puberty			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	1 / 16 (6.25%)
occurrences (all)	0	1	2
Back pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			

subjects affected / exposed	0 / 28 (0.00%)	2 / 34 (5.88%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Muscle atrophy			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Scoliosis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Coccydynia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	2 / 34 (5.88%)	4 / 16 (25.00%)
occurrences (all)	0	2	4
Corona virus infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 28 (0.00%)	4 / 34 (11.76%)	2 / 16 (12.50%)
occurrences (all)	0	5	2
Rhinitis			
subjects affected / exposed	0 / 28 (0.00%)	5 / 34 (14.71%)	2 / 16 (12.50%)
occurrences (all)	0	8	5
Influenza			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	1 / 16 (6.25%)
occurrences (all)	0	1	1

Gastroenteritis			
subjects affected / exposed	0 / 28 (0.00%)	2 / 34 (5.88%)	2 / 16 (12.50%)
occurrences (all)	0	2	3
Conjunctivitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	1 / 16 (6.25%)
occurrences (all)	0	1	2
Lower respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	3 / 34 (8.82%)	0 / 16 (0.00%)
occurrences (all)	0	4	0
Eye infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Gastroenteritis viral			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Hordeolum			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Febrile infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Haemophilus infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Infected bite			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oral fungal infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Otitis media			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	3 / 34 (8.82%)	1 / 16 (6.25%)
occurrences (all)	0	6	2
Sinusitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Tracheitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Varicella			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hand-foot-and-mouth Disease			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1



Localised Infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Medical Device Site Infection			
subjects affected / exposed	0 / 28 (0.00%)	2 / 34 (5.88%)	0 / 16 (0.00%)
occurrences (all)	0	5	0
Onychomycosis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Oral Candidiasis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Skin Candida			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Viral Infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 34 (2.94%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vulvovaginal Mycotic Infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Wound infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 28 (3.57%)	6 / 34 (17.65%)	1 / 16 (6.25%)
occurrences (all)	1	8	1
Candida infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 34 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Furuncle			

subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Postoperative wound infection subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Stoma site infection subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Metabolism and nutrition disorders			
Iron deficiency subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 2	0 / 16 (0.00%) 0
Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 1	0 / 16 (0.00%) 0
Dehydration subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Folate deficiency subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Hypercholesterolaemia subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Malnutrition subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 34 (0.00%) 0	0 / 16 (0.00%) 0
Decreased appetite subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	3 / 34 (8.82%) 4	0 / 16 (0.00%) 0
Refeeding syndrome subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 1	0 / 16 (0.00%) 0

Vitamin C deficiency subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 34 (2.94%) 1	0 / 16 (0.00%) 0
--	---------------------	---------------------	---------------------

<b>Non-serious adverse events</b>	Open-label Arimoclomol (48- month OLE Phase)	Open-label Arimoclomol (36- month pediatric substudy)	
Total subjects affected by non-serious adverse events subjects affected / exposed	38 / 41 (92.68%)	5 / 5 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Haemangioma of liver subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	1 / 5 (20.00%) 1	
Vascular disorders Haematoma subjects affected / exposed occurrences (all)  Haemorrhage subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3  1 / 41 (2.44%) 1	0 / 5 (0.00%) 0  0 / 5 (0.00%) 0	
Surgical and medical procedures Gastrostomy subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	0 / 5 (0.00%) 0	
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)  Medical device site reaction subjects affected / exposed occurrences (all)  Fatigue subjects affected / exposed occurrences (all)  Malaise subjects affected / exposed occurrences (all)  Abasia	4 / 41 (9.76%) 9  2 / 41 (4.88%) 3  2 / 41 (4.88%) 2  1 / 41 (2.44%) 3	1 / 5 (20.00%) 9  0 / 5 (0.00%) 0  0 / 5 (0.00%) 0  0 / 5 (0.00%) 0	

subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Gait disturbance		
subjects affected / exposed	1 / 41 (2.44%)	1 / 5 (20.00%)
occurrences (all)	1	1
Influenza like illness		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Local swelling		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Medical device site haemorrhage		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Medical device site ulcer		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Oedema peripheral		
subjects affected / exposed	1 / 41 (2.44%)	1 / 5 (20.00%)
occurrences (all)	1	1
Unevaluable event		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Asthenia		
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0
Medical Device Site Dermatitis		
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0
Pain		
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0
Peripheral Swelling		
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0
Secretion Discharge		

subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Disease progression			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	2	
Temperature regulation disorder			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Immune system disorders			
Renal abscess			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Seasonal allergy			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Drug Hypersensitivity			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Food Allergy			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Social circumstances			
Convalescent			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Perineal rash			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Premenstrual Syndrome			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Menstruation irregular			

subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 41 (17.07%)	2 / 5 (40.00%)	
occurrences (all)	9	8	
Epistaxis			
subjects affected / exposed	6 / 41 (14.63%)	0 / 5 (0.00%)	
occurrences (all)	8	0	
Oropharyngeal pain			
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)	
occurrences (all)	4	0	
Asthma			
subjects affected / exposed	2 / 41 (4.88%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Interstitial lung disease			
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Aspiration			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Bronchial hyperreactivity			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Increased upper airway secretion			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Lung disorder			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Pneumonia aspiration			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Respiratory tract inflammation			

subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Bronchospasm			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dysphonia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Nasal Congestion			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Productive Cough			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	2 / 41 (4.88%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Anxiety			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Attention deficit/hyperactivity disorder			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Illusion			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Initial insomnia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Insomnia			

subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Aggression			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Agitation			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hallucination, auditory			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hallucination, visual			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Investigations			
Weight decreased			
subjects affected / exposed	6 / 41 (14.63%)	0 / 5 (0.00%)	
occurrences (all)	8	0	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 41 (7.32%)	2 / 5 (40.00%)	
occurrences (all)	3	3	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 41 (4.88%)	3 / 5 (60.00%)	
occurrences (all)	2	3	
Blood triglycerides increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Blood creatine increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Blood lactate dehydrogenase increased			



subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Blood magnesium increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Eosinophil count increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Gastric pH decreased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Platelet count decreased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Vitamin D decreased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Body Temperature Abnormal			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Body Temperature Increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
C-reactive Protein Increased			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Blood iron decreased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Ultrasound liver abnormal			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Contusion			

subjects affected / exposed	4 / 41 (9.76%)	0 / 5 (0.00%)	
occurrences (all)	4	0	
Laceration			
subjects affected / exposed	3 / 41 (7.32%)	0 / 5 (0.00%)	
occurrences (all)	5	0	
Expired product administered			
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Fall			
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Stoma site hypergranulation			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Eye contusion			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Eye injury			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Joint dislocation			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Lip injury			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	1 / 41 (2.44%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Traumatic haemorrhage			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Eschar			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Head Injury			

subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	0 / 5 (0.00%) 0	
Injury subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	0 / 5 (0.00%) 0	
Ligament Sprain subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	0 / 5 (0.00%) 0	
Tooth Injury subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	0 / 5 (0.00%) 0	
Congenital, familial and genetic disorders Phimosis subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	0 / 5 (0.00%) 0	
Nervous system disorders Epilepsy subjects affected / exposed occurrences (all)	7 / 41 (17.07%) 8	0 / 5 (0.00%) 0	
Seizure subjects affected / exposed occurrences (all)	6 / 41 (14.63%) 11	0 / 5 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	4 / 41 (9.76%) 15	0 / 5 (0.00%) 0	
Cataplexy subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3	0 / 5 (0.00%) 0	
Dystonia subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3	0 / 5 (0.00%) 0	
Lethargy subjects affected / exposed occurrences (all)	2 / 41 (4.88%) 3	0 / 5 (0.00%) 0	
Tremor			

subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	4	0	
Dizziness			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Quadriparesis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Ageusia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Balance disorder			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Coordination abnormal			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Disturbance in attention			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Droling			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Dysmetria			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hypertonia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hypotonia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Motor dysfunction			

subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Muscle spasticity			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Neurological decompensation			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Partial seizures			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Peripheral sensorimotor neuropathy			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Quadriplegia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Speech disorder			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Tonic convulsion			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Aphasia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Cognitive Disorder			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Memory Impairment			

subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Migraine			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Peroneal Nerve Palsy			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Petit Mal Epilepsy			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	3 / 41 (7.32%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Splenomegaly			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Anaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Eosinophilia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Excessive cerumen production			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Deafness Neurosensory			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Deafness Unilateral			

subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Ear Pain			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Middle ear effusion			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Tympanic membrane perforation			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Eye disorders			
Corneal epithelium defect			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Corneal opacity			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Saccadic eye movement			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Pupils Unequal			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Diplopia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 41 (24.39%)	3 / 5 (60.00%)	
occurrences (all)	27	4	
Vomiting			

subjects affected / exposed	5 / 41 (12.20%)	2 / 5 (40.00%)
occurrences (all)	7	6
Constipation		
subjects affected / exposed	5 / 41 (12.20%)	2 / 5 (40.00%)
occurrences (all)	6	3
Dysphagia		
subjects affected / exposed	3 / 41 (7.32%)	0 / 5 (0.00%)
occurrences (all)	3	0
Abdominal distension		
subjects affected / exposed	1 / 41 (2.44%)	1 / 5 (20.00%)
occurrences (all)	1	1
Anal fissure		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Anal haemorrhage		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Gastrointestinal disorder		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Gastrooesophageal reflux disease		
subjects affected / exposed	1 / 41 (2.44%)	1 / 5 (20.00%)
occurrences (all)	1	1
Inflammatory bowel disease		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Inguinal hernia		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Nausea		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Salivary hypersecretion		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Abdominal Pain Upper		



subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Abdominal Discomfort			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Aphthous Ulcer			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dental Caries			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Lip Dry			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Mouth Cyst			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Odynophagia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Tongue ulceration			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	3	
Anorectal disorder			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hepatic Lesion			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hepatomegaly			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	

Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	5 / 41 (12.20%)	0 / 5 (0.00%)	
occurrences (all)	5	0	
Acne			
subjects affected / exposed	3 / 41 (7.32%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Dry skin			
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Decubitus ulcer			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Acanthosis nigricans			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Alopecia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Angiokeratoma			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Blister			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Dermatitis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Dermatitis allergic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Dermatitis diaper			
subjects affected / exposed	1 / 41 (2.44%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Rash			

subjects affected / exposed	1 / 41 (2.44%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Skin lesion			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Umbilical discharge			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Angioedema			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dandruff			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Henoch-Schonlein Purpura			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Urticaria			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Oliguria			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Precocious puberty			
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	2 / 41 (4.88%)	1 / 5 (20.00%)	
occurrences (all)	2	1	
Back pain			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Pain in extremity			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Muscle atrophy			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Muscular weakness			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Scoliosis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Coccydynia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	8 / 41 (19.51%)	1 / 5 (20.00%)	
occurrences (all)	18	6	
Corona virus infection			
subjects affected / exposed	8 / 41 (19.51%)	0 / 5 (0.00%)	
occurrences (all)	8	0	
Bronchitis			

subjects affected / exposed	7 / 41 (17.07%)	0 / 5 (0.00%)
occurrences (all)	7	0
Rhinitis		
subjects affected / exposed	5 / 41 (12.20%)	0 / 5 (0.00%)
occurrences (all)	14	0
Influenza		
subjects affected / exposed	4 / 41 (9.76%)	0 / 5 (0.00%)
occurrences (all)	6	0
Gastroenteritis		
subjects affected / exposed	4 / 41 (9.76%)	1 / 5 (20.00%)
occurrences (all)	4	1
Conjunctivitis		
subjects affected / exposed	2 / 41 (4.88%)	1 / 5 (20.00%)
occurrences (all)	7	1
Lower respiratory tract infection		
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	4	0
Eye infection		
subjects affected / exposed	2 / 41 (4.88%)	1 / 5 (20.00%)
occurrences (all)	3	1
Gastroenteritis viral		
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	3	0
Urinary tract infection		
subjects affected / exposed	2 / 41 (4.88%)	1 / 5 (20.00%)
occurrences (all)	3	1
Fungal infection		
subjects affected / exposed	2 / 41 (4.88%)	1 / 5 (20.00%)
occurrences (all)	2	1
Hordeolum		
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	2	0
Tonsillitis		
subjects affected / exposed	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	2	0
Ear infection		

subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	4	0
Febrile infection		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Fungal skin infection		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Haemophilus infection		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Infected bite		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Oral fungal infection		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Otitis media		
subjects affected / exposed	1 / 41 (2.44%)	1 / 5 (20.00%)
occurrences (all)	1	1
Pharyngitis		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Pneumonia		
subjects affected / exposed	1 / 41 (2.44%)	1 / 5 (20.00%)
occurrences (all)	1	2
Respiratory tract infection		
subjects affected / exposed	1 / 41 (2.44%)	1 / 5 (20.00%)
occurrences (all)	1	1
Sinusitis		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Staphylococcal infection		
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	0
Tracheitis		

subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Varicella			
subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hand-foot-and-mouth Disease			
subjects affected / exposed	0 / 41 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Localised Infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Medical Device Site Infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Onychomycosis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Oral Candidiasis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Skin Candida			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Viral Infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal Mycotic Infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Wound infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	

Upper respiratory tract infection subjects affected / exposed occurrences (all)	9 / 41 (21.95%) 17	2 / 5 (40.00%) 5	
Candida infection subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	1 / 5 (20.00%) 1	
Furuncle subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	1 / 5 (20.00%) 1	
Postoperative wound infection subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	1 / 5 (20.00%) 1	
Stoma site infection subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	1 / 5 (20.00%) 1	
Metabolism and nutrition disorders			
Iron deficiency subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3	0 / 5 (0.00%) 0	
Vitamin D deficiency subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3	0 / 5 (0.00%) 0	
Dehydration subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1	0 / 5 (0.00%) 0	
Folate deficiency subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1	0 / 5 (0.00%) 0	
Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1	0 / 5 (0.00%) 0	
Hypokalaemia subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1	0 / 5 (0.00%) 0	
Malnutrition			



subjects affected / exposed	1 / 41 (2.44%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Refeeding syndrome			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Vitamin C deficiency			
subjects affected / exposed	0 / 41 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 August 2016	Protocol version 4.0: Specification of "end of trial" at 36 months (based on regulatory feedback). The secondary objectives and the corresponding endpoints were updated to include the evaluation of therapeutic response and safety at 36 months. CGI-S and CGI-I added as secondary endpoints as requested by the FDA.
11 May 2017	Protocol version 5.0: Biomarker endpoints updated: 7-ketocholesterol removed from the assessments due to stability problems with the analyte. Glycosphingolipids and sphingoid bases added as endpoints. Sample size updated to include up to 52 randomised patients.
13 March 2018	Protocol version 6.0: Change of primary endpoint to the 5-domain NPCCSS instead of the full scale NPCCSS upon recommendation from the FDA. This was done in order to reduce the variability and thereby increase the robustness of the primary endpoint analysis. The selection of domains was based upon the clinical importance as verified by research conducted by Orphazyme in collaboration with therapeutic area experts, patients, and families. Secondary endpoints ranked to specify "key secondary endpoints" and "other secondary endpoints" to indicate the level of importance. The following key secondary endpoints included: responder analyses (on CGI-I score and 5-domain NPCCSS) and time to worsening (defined as the time until the patient reaches the predefined MCT of 2 points on the 5- domain NPCCSS) added as key secondary endpoints based on regulatory feedback. For the FDA submission, CGI-score was to be considered a coprimary endpoint. The original primary endpoint, change in full scale NPCCSS (apart from hearing domains) at 12 months, changed to be a key secondary endpoint. Additional secondary endpoints added: - Change in 5-domain NPCCSS score at 6, 18, 24, 30, and 36 months;- Change in full scale NPCCSS score apart from hearing domains (i.e. Hearing and Auditory Brainstem Response) at 6, 18, 24, 30, and 36 months;- Responder analyses for CGI-I and NPCCSS, respectively, at 6, 18, 24, 30, and 36 months;- Proportion of patients worsening at 18, 24, 30, and 36 months. Clarification that the exploratory endpoint for NPC disease progression rate is based on NPCCSS apart from hearing domains. Definition of baseline clarified to be the latest assessment prior to randomisation. Interim analysis included, planned to be performed once approximately 50% of the ongoing patients had received 6 months of open-label treatment with arimoclomol. Clarification of analysis set definitions
12 July 2018	Protocol version 7.0: Changes implemented which were only relevant for the open-label extension phase: Collection of a PK sample was added at Visit 8 (after 12 months of open-label treatment). It was clarified that the DSMB was only to review safety data during the double-blind phase of the trial.

09 July 2019	<p>Protocol version 8.0: Addition of the Lyso-SM-509 biomarker. Additional changes which were only relevant for the open-label extension phase: Since a marketing authorization had not been obtained and efficacy and/or safety of arimoclomol did not require trial termination, the original 2-year OLE phase of the trial was extended with 2 years to a total duration of 60 months for the full trial (12 months double-blind and 48 months OLE). Accordingly, 4 additional visits (Visits 10, 11, 12, and 13 at Months 36, 42, 48, and 54 in the full trial) were added throughout the protocol, and end of the OLE phase (at Month 60 in the full trial) was changed to Visit 14. Furthermore, the corresponding timepoints were added to the secondary objectives and endpoints.</p> <ul style="list-style-type: none"> <li>• Based upon the observations from the double-blind part of the trial, it was found relevant to continue analyzing the levels of unesterified cholesterol, HSP70, and GSLs in the OLE phase. In addition, lyso-SM-509, a promising new biomarker for NPC, was added as a potential marker of the disease progression. The analysis of NPC-1 active protein was omitted.</li> </ul>
09 June 2020	<p>Protocol version 9.0: The period of using contraception after last dose of IMP was extended for female patients from 1 to 3 weeks to cover 5 half-lives of the arimoclomol metabolites. The CRO for the trial was changed from Orion Clinical Services to Worldwide Clinical Trials, and the vendor for the statistical analyses was changed from Orion Clinical Services to Larix A/S.</p>
25 September 2020	<p>Protocol version 10.0: It was added that dose adjustment due to increased serum creatinine could be temporary and that subsequent dose increase had to be discussed with the medical monitor (or delegate). • Safety and tolerability were deleted as primary endpoint. This had been included as primary endpoint by mistake when adding the pediatric sub-study to the protocol. The primary objective of the pediatric sub-study is safety and tolerability; however, the pediatric sub-study has no primary endpoint. • Clarification in wording regarding AE/SAE reporting procedures was made. The names of data management vendors were removed to avoid later amendments due to changes in vendors.</p>
21 June 2022	<p>The name of the sponsor was changed from Orphazyme A/S to KemPharm Denmark A/S (taking over from Orphazyme A/S on 01-Jun-2022) throughout the protocol</p>

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported