Clinical trial results:
A Phase 2, Multiple Dose, Open-Label, Parallel-Group, Active Controlled, Safety, Tolerability, Pharmacokinetic and Pharmacodynamic Study of ACP-001 in Adult Patients with Growth Hormone Deficiency (AGHD)

Summary

EudraCT number	2010-021523-28
Trial protocol	AT DK SE DE IT
Global end of trial date	24 May 2011

Results information

Result version number	v1 (current)
This version publication date	31 May 2019
First version publication date	31 May 2019

Trial information

Trial identification

Sponsor protocol code	ACP-001 CT-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01247675
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ascendis Pharma A/S
Sponsor organisation address	Tuborg Boulevard 12, Hellerup, Denmark, DK 2900
Public contact	Michael Beckert, MD, Ascendis Pharma A/S, mb@ascendispharma.com
Scientific contact	Michael Beckert, MD, Ascendis Pharma A/S, mb@ascendispharma.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 May 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 May 2011
Global end of trial reached?	Yes
Global end of trial date	24 May 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the safety and tolerability of ACP-001 under multiple-dose conditions in adult patients with Growth Hormone Deficiency

Protection of trial subjects:

Institutional review board and independent ethics committee approval as well as signed informed consent from subjects was obtained prior to any trial-specific procedures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 13
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Denmark: 6
Worldwide total number of subjects	37
EEA total number of subjects	37

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	28
From 65 to 84 years	9

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 4 reference centers in Sweden, Denmark, Germany and Italy. Subject screening was initiated in October 2010 and the final subject visit was in May 2011.

Pre-assignment

Screening details:

Prior to randomization, study subjects entered a 14 to 21 day wash out period following cessation of daily growth hormone therapy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	ACP-001, 0.02 mg hGH/kg/wk

Arm description:

Once weekly subcutaneous injection of ACP-001 equivalent to 0.02 mg hGH/kg/week for 4 weeks

Arm type	Experimental
Investigational medicinal product name	TransCon hGH
Investigational medicinal product code	ACP-001
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

ACP-001 (TransCon hGH) is injected subcutaneously once-a-week using a syringe and 30-gauge needle. The lyophilized drug product is reconstituted with sterile water for injection prior to use.

Arm title	ACP-001, 0.04 mg hGH/kg/wk

Arm description:

Once weekly subcutaneous injection of ACP-001 equivalent to 0.04 mg hGH/kg/week for 4 weeks

Arm type	Experimental
Investigational medicinal product name	TransCon hGH
Investigational medicinal product code	ACP-001
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

ACP-001 (TransCon hGH) is injected subcutaneously once-a-week using a syringe and 30-gauge needle. The lyophilized drug product is reconstituted with sterile water for injection prior to use.

Arm title	ACP-001, 0.08 mg hGH/kg/wk

Arm description:

Once weekly subcutaneous injection of ACP-001 equivalent to 0.08 mg hGH/kg/week for 4 weeks

Arm type	Experimental

Investigational medicinal product name	TransCon hGH
Investigational medicinal product code	ACP-001
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

ACP-001 (TransCon hGH) is injected subcutaneously once-a-week using a syringe and 30-gauge needle. The lyophilized drug product is reconstituted with sterile water for injection prior to use.

Arm title	Omnitrope, 0.04 mg hGH/kg/wk

Arm description:

Once daily subcutaneous injection of human Growth Hormone (Omnitrope) equivalent to 0.04 mg hGH/kg/week for 4 weeks

Arm type	Active comparator
Investigational medicinal product name	Omnitrope
Investigational medicinal product code	
Other name	Human growth hormone
Pharmaceutical forms	Solution for injection in cartridge
Routes of administration	Subcutaneous use

Dosage and administration details:

Omnitrope is delivered once-daily by subcutaneous injection. The drug product solution is provided in a glass cartridge ready for use in the Omnitrope Pen 5.

Number of subjects in period 1	ACP-001, 0.02 mg hGH/kg/wk	ACP-001, 0.04 mg hGH/kg/wk	ACP-001, 0.08 mg hGH/kg/wk
Started	10	10	9
Completed	8	8	9
Not completed	2	2	0
Consent withdrawn by subject	1	-	-
Physician decision	1	-	-
Adverse event, non-fatal	-	2	-

Number of subjects in period 1	Omnitrope, 0.04 mg hGH/kg/wk
Started	8
Completed	8
Not completed	0
Consent withdrawn by subject	-
Physician decision	-
Adverse event, non-fatal	-

Baseline characteristics

Reporting groups	
Reporting group title	ACP-001, 0.02 mg hGH/kg/wk
Reporting group description:	
Once weekly subcutaneous injection of ACP-001 equivalent to 0.02 mg hGH/kg/week for 4 weeks	
Reporting group title	ACP-001, 0.04 mg hGH/kg/wk
Reporting group description:	
Once weekly subcutaneous injection of ACP-001 equivalent to 0.04 mg hGH/kg/week for 4 weeks	
Reporting group title	ACP-001, 0.08 mg hGH/kg/wk
Reporting group description:	
Once weekly subcutaneous injection of ACP-001 equivalent to 0.08 mg hGH/kg/week for 4 weeks	
Reporting group title	Omnitrope, 0.04 mg hGH/kg/wk
Reporting group description:	
Once daily subcutaneous injection of human Growth Hormone (Omnitrope) equivalent to 0.04 mg hGH/kg/week for 4 weeks	

Reporting group values	ACP-001, 0.02 mg hGH/kg/wk	ACP-001, 0.04 mg hGH/kg/wk	ACP-001, 0.08 mg hGH/kg/wk
Number of subjects	10	10	9
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	55.7	45.9	51.6
standard deviation	± 12.6	± 15.0	± 18.1
Gender categorical			
Units: Subjects			
Female	5	6	5
Male	5	4	4

Reporting group values	Omnitrope, 0.04 mg hGH/kg/wk	Total	
Number of subjects	8	37	
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)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
arithmetic mean	44.0		
standard deviation	± 15.7	-	
Gender categorical			
Units: Subjects			
Female	3	19	
Male	5	18	

End points

End points reporting groups

Reporting group title	ACP-001, 0.02 mg hGH/kg/wk
Reporting group description:	
Once weekly subcutaneous injection of ACP-001 equivalent to 0.02 mg hGH/kg/week for 4 weeks	
Reporting group title	ACP-001, 0.04 mg hGH/kg/wk
Reporting group description:	
Once weekly subcutaneous injection of ACP-001 equivalent to 0.04 mg hGH/kg/week for 4 weeks	
Reporting group title	ACP-001, 0.08 mg hGH/kg/wk
Reporting group description:	
Once weekly subcutaneous injection of ACP-001 equivalent to 0.08 mg hGH/kg/week for 4 weeks	
Reporting group title	Omnitrope, 0.04 mg hGH/kg/wk
Reporting group description:	
Once daily subcutaneous injection of human Growth Hormone (Omnitrope) equivalent to 0.04 mg hGH/kg/week for 4 weeks	

Primary: Number of Subjects Reporting Local Tolerability Events (Assessed by the Patient and Investigator)

End point title	Number of Subjects Reporting Local Tolerability Events (Assessed by the Patient and Investigator)[1]
End point description:	
Assessment of local tolerability was performed by examining injection sites by the investigator during study visits, and on the basis of records in the Patient Diary. Assessments included erythema, swelling, or pain.	
End point type	Primary
End point timeframe:	
Start of study treatment through Week 4	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Nine subjects experienced at least one injection site reaction and there was no clear difference in these reactions between ACP-001 and Omnitrope treated subjects.	

End point values	ACP-001, 0.02 mg hGH/kg/wk	ACP-001, 0.04 mg hGH/kg/wk	ACP-001, 0.08 mg hGH/kg/wk	Omnitrope, 0.04 mg hGH/kg/wk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	9	8
Units: Number of subjects with any symptom	3	3	2	1

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of Treatment Emergent Anti-hGH Binding Antibody Formation

End point title	Incidence of Treatment Emergent Anti-hGH Binding Antibody

	Formation[2]

End point description:

Number of subjects with treatment emergent anti-hGH binding antibodies

End point type	Primary

End point timeframe:

Start of study treatment through Day 42

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no Treatment Emergent anti-hGH binding antibodies in any of the treatment arms.

End point values	ACP-001, 0.02 mg hGH/kg/wk	ACP-001, 0.04 mg hGH/kg/wk	ACP-001, 0.08 mg hGH/kg/wk	Omnitrope, 0.04 mg hGH/kg/wk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	9	8
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of hGH

End point title	Cmax of hGH

End point description:

As part of the following endpoint:
Pharmacokinetic (PK) profile of serum human Growth Hormone (hGH) from ACP-001 treated dose groups compared to the PK profile of hGH from the daily Omnitrope treated group.
Cmax (maximum value of concentration) values at Week 4

End point type	Secondary

End point timeframe:

Days 22 to 29

End point values	ACP-001, 0.02 mg hGH/kg/wk	ACP-001, 0.04 mg hGH/kg/wk	ACP-001, 0.08 mg hGH/kg/wk	Omnitrope, 0.04 mg hGH/kg/wk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	8	9	8
Units: ng/mL				
arithmetic mean (standard deviation)	1.2 (± 0.8)	1.9 (± 0.9)	3.8 (± 2.0)	2.0 (± 1.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Emax of IGF-I

End point title	Emax of IGF-I

End point description:

As part of the following endpoint:
Pharmacodynamic (PD) response of serum Insulin-like Growth Factor-I (IGF-I) from ACP-001 treated dose groups compared to the PD response of IGF-I from the daily Omnitrope treated group.
Emax (maximum observed response) values at Week 4

End point type	Secondary

End point timeframe:

Days 22 to 29

End point values	ACP-001, 0.02 mg hGH/kg/wk	ACP-001, 0.04 mg hGH/kg/wk	ACP-001, 0.08 mg hGH/kg/wk	Omnitrope, 0.04 mg hGH/kg/wk
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	8	9	8
Units: ng/mL				
arithmetic mean (standard deviation)	71.8 (± 26.9)	108.6 (± 91.7)	125.6 (± 70.1)	109.8 (± 37.1)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Reported Adverse Events include events starting on or after Day 0 and ending on or before Day 42.	
Adverse event reporting additional description:	
A subject with more than one finding in a specific category was only counted once.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups	
Reporting group title	ACP-001, 0.02 mg hGH/kg/wk
Reporting group description:	
Once weekly subcutaneous injection of ACP-001 equivalent to 0.02 mg hGH/kg/week for 4 weeks	
Reporting group title	ACP-001, 0.04 mg hGH/kg/wk
Reporting group description:	
Once weekly subcutaneous injection of ACP-001 equivalent to 0.04 mg hGH/kg/week for 4 weeks	
Reporting group title	ACP-001, 0.08 mg hGH/kg/wk
Reporting group description:	
Once weekly subcutaneous injection of ACP-001 equivalent to 0.08 mg hGH/kg/week for 4 weeks	
Reporting group title	Omnitrope, 0.04 mg hGH/kg/wk
Reporting group description:	
Once daily subcutaneous injection of human Growth Hormone (Omnitrope) equivalent to 0.04 mg hGH/kg/week for 4 weeks	

Serious adverse events	ACP-001, 0.02 mg hGH/kg/wk	ACP-001, 0.04 mg hGH/kg/wk	ACP-001, 0.08 mg hGH/kg/wk
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Respiratory, thoracic and mediastinal disorders			
Pleuritic Pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 9 (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
Endocrine disorders			
Severe Adrenal Crisis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 9 (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

Serious adverse events	Omnitrope, 0.04 mg hGH/kg/wk		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Respiratory, thoracic and mediastinal disorders			
Pleuritic Pain			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Severe Adrenal Crisis			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	ACP-001, 0.02 mg hGH/kg/wk	ACP-001, 0.04 mg hGH/kg/wk	ACP-001, 0.08 mg hGH/kg/wk
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 10 (60.00%)	9 / 10 (90.00%)	7 / 9 (77.78%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	2 / 10 (20.00%)	3 / 10 (30.00%)	2 / 9 (22.22%)
occurrences (all)	2	3	7
General disorders and administration site conditions			
Application site erythema			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Application site induration			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0

Application site pruritus			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Asthenia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Condition aggravated			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	0	3	3
Edema peripheral			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Fatigue			
subjects affected / exposed	3 / 10 (30.00%)	3 / 10 (30.00%)	1 / 9 (11.11%)
occurrences (all)	8	4	4
Influenza like illness			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Injection site pain			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	2	4	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	3
Abdominal pain upper			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
Dyspepsia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Nausea			

subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	2 / 9 (22.22%)
occurrences (all)	0	3	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Nasal congestion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 10 (10.00%)	3 / 10 (30.00%)	2 / 9 (22.22%)
occurrences (all)	1	4	2
Rales			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	1	1	1
Rhinorrhoea			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	1	1	1
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Insomnia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	3	0	0
Stress			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Hematuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	2	2	2
Back pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	2 / 9 (22.22%)
occurrences (all)	1	0	3
Myalgia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	3
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	2
Nasopharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	2 / 9 (22.22%)
occurrences (all)	0	2	2
Pharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	2

Non-serious adverse events	Omnitrope, 0.04 mg hGH/kg/wk		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	4		
General disorders and administration site conditions			

Application site erythema			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Application site induration			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Application site pruritus			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Condition aggravated			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Edema peripheral			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	12		
Influenza like illness			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Injection site pain			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Diarrhoea			

subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Rales			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Stress			

subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	3		
Renal and urinary disorders			
Hematuria			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28196799