Clinical trial results:
A Phase I/II Study of Lenalidomide in Patients with Chronic Myelomonocytic Leukemia

Summary

EudraCT number	2009-017147-33
Trial protocol	AT
Global end of trial date	08 February 2016

Results information

Result version number	v1
This version publication date	25 February 2017
First version publication date	25 February 2017

Trial information

Trial identification

Sponsor protocol code	AGMT_CMML1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01368757
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AGMT
Sponsor organisation address	Gentzgasse 60/20, Wien, Austria, 1180
Public contact	Daniela Wolkersdorfer, AGMT gemeinnützige GmbH, +43 6641422504, d.wolkersdorfer@agmt.at
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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	08 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 February 2016
Global end of trial reached?	Yes
Global end of trial date	08 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase I:
The primary objective of the phase I trial is to determine the MTD (maximum tolerated dose) of lenalidomide.

Phase II:
The primary objective of the phase II trial is to determine the hematologic response achieved with lenalidomide administered in subjects at the MTD determined in phase I.

Protection of trial subjects:

Safety assessments were done weekly in cycle 1, every second week in cycle 2 and on day 1 of the following cycles.
Patients were counselled before each cycle of Lenalidomide e.g. about pregnancy precautions and the potential risks of fetal exposure to Lenalidomide.

Background therapy:

None.

Evidence for comparator: -

Actual start date of recruitment	14 July 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	Austria: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	3
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between July 2010 and January 2014 20 patients were recruited at 8 sites in Austria. Patients were enrolled using a traditional "3+3 " design. Due to the very prolonged recruitment period in phase I, it was discussed and decided not to start phase II of the study. No further patients will were enrolled into AGMT_CMML 1.

Pre-assignment

Screening details:

Eligible patients had a confirmed diagnosis of CMML according to the WHO criteria. Pretreatment was permitted.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 5 mg

Arm description:

Daily dose of lenalidomide: 5 mg.

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

Dosage and administration details:

Lenalidomide (5 mg) was administered daily in a 28 days cycle. All subjects were planned to continue on study drug until disease progression, unacceptable toxicity or treatment discontinuation for any other reason.

Arm title	Cohort 10 mg

Arm description:

Daily dose of lenalidomide: 10 mg.

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

Dosage and administration details:

Lenalidomide (10 mg) was administered daily in a 28 days cycle. All subjects were planned to continue on study drug until disease progression, unacceptable toxicity or treatment discontinuation for any other reason.

Arm title	Cohort 15 mg

Arm description:

Daily dose of lenalidomide: 15 mg.

Arm type	Experimental

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

Dosage and administration details:

Lenalidomide (15 mg) was administered daily in a 28 days cycle. All subjects were planned to continue on study drug until disease progression, unacceptable toxicity or treatment discontinuation for any other reason.

Number of subjects in period 1	Cohort 5 mg	Cohort 10 mg	Cohort 15 mg
Started	6	6	8
Completed	2	2	1
Not completed	4	4	7
Adverse event, serious fatal	-	-	2
Adverse event, non-fatal	4	4	5

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	20	20	
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			
median	72		
full range (min-max)	59 to 81	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	17	17	

End points

End points reporting groups

Reporting group title	Cohort 5 mg
Reporting group description: Daily dose of lenalidomide: 5 mg.	
Reporting group title	Cohort 10 mg
Reporting group description: Daily dose of lenalidomide: 10 mg.	
Reporting group title	Cohort 15 mg
Reporting group description: Daily dose of lenalidomide: 15 mg.	

Primary: Evaluation of maximum tolerated dose (MTD)

End point title	Evaluation of maximum tolerated dose (MTD)[1]

End point description:

The MTD (maximum tolerated dose) of lenalidomide is defined as the highest dose level at which no more than 1 out of 6 subjects experience a dose-limiting toxicity (DLT) during the first cycle of administration.

Dose limiting toxicity is defined as inability to deliver lenalidomide in cycle 1 due to drug related toxicity as outlined below:
o any grade 3/4 non-hematologic toxicity (excluding alopecia)
o febrile neutropenia
o any grade 4 neutropenia lasting for ≥ 7 days
o grade 4 thrombocytopenia

End point type	Primary

End point timeframe:

28 days
End of cycle 1 of each patient

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is provided as this is an one armed, open label, non-comperative study.
Two out of 6 patients each in the 10 mg cohort and the 15 mg cohort developed DLTs. Therefore 5 mg lenalidomide was identified as the MTD.

End point values	Cohort 5 mg	Cohort 10 mg	Cohort 15 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: Patients				
DLT in cycle 1	0	2	2	
No DLT in cycle 1	6	4	4	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All patients having received at least one dose of the study medication were followed for adverse events from treatment start to 28 days after discontinuing study treatment or completion of study.

Adverse event reporting additional description:

Laboratory test value abnormalities as such were not reported on the AE page of the CRF as adverse events, unless there was an associated clinical condition for which the patient was given treatment or concomitant treatment altered, it was considered to be a serious adverse event, or the patient was permanently discontinued from study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 20 (70.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Blastic plasmacytoid dendritic cell neoplasia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypersensitivity vasculitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Temporal arteritis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial tachycardia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cyanosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

Disseminated intravascular coagulation				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal tenesmus				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Swelling face				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal impairment				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary retention				

subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	1 / 2		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal polyp			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Vascular disorders			
Angiopathy			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

Carotid arteriosclerosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gingival bleeding			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Haematochezia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Haematoma			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Haemorrhagic vasculitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Surgical and medical procedures			
Lipoma excision			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	7 / 20 (35.00%)		
occurrences (all)	11		
Injection site erythema			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Mucosal inflammation			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Night sweats			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	4		
Oedema			

subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Pyrexia			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	15		
Reproductive system and breast disorders			
Cervix disorder			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Bronchitis bacterial			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	6		
Productive cough			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Respiratory distress			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Respiratory failure			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Dyspnoea			

subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Dyspnoea exertional			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Mental disorder			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Blood uric acid increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Chlamydia test positive			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Ligament sprain			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Vaccination complication			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Tricuspid valve disease			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Insomnia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Neuropathy peripheral			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Polyneuropathy			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Tremor			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	7		
Febrile neutropenia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Leukocytosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	6		
Lymphopenia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	6 / 20 (30.00%)		
occurrences (all)	8		
Thrombocytopenia			
subjects affected / exposed	10 / 20 (50.00%)		
occurrences (all)	27		
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Vertigo			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Eye disorders			

Cataract			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Chorioretinal disorder			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Macular degeneration			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Ascites			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	7		
Diarrhoea			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	9		
Dry mouth			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Epigastric discomfort			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastroenteritis			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal disorder			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal hypermotility			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Herpes simplex			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Ileal ulcer			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Oral mucosa haematoma			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Rectal tenesmus			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Hyperbilirubinaemia			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		

Skin and subcutaneous tissue disorders			
Actinic elastosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Hypersensitivity vasculitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Petechiae			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Psoriasis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	5		
Rosacea			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Skin lesion			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Skin plaque			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Skin ulcer			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Renal and urinary disorders			

Nocturia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Renal pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	6		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Bursitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Sjogren's syndrome			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	10		
Pneumonia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Transfusion reaction			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Bronchitis			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Folate deficiency			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Hyperuricaemia			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Hypokalaemia			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	4		

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