Clinical trial results:
Phase 3B, Randomized Trail of Revlimid® (Lenalidomide) Versus Placebo Maintenance Therapy Following Melphalan Prednisone Velcade (Bortezomib) Induction Therapy In Newly Diagnosed Multiple Myeloma

Summary

EudraCT number	2013-001729-26
Trial protocol	BE ES IT FR GR
Global end of trial date	12 October 2020

Results information

Result version number	v2 (current)
This version publication date	29 April 2023
First version publication date	28 October 2021
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CC-5013-MM-026

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	12 October 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Investigate efficacy and safety of maintenance therapy with lenalidomide versus placebo after melphalan prednisone Velcade (MPV) induction therapy in subjects with newly-diagnosed multiple myeloma (NDMM)

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 May 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Belgium: 2
Worldwide total number of subjects	46
EEA total number of subjects	46

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)	1
From 65 to 84 years	45
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

46 participants randomized and treated

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Lenalidomide

Arm description:

10mg/day PO from Days 1 to 21 (given in 28-day cycles)

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

Dosage and administration details:

10mg/day from Days 1 to 21 (given in 28-day cycles)

Arm title	Placebo

Arm description:

Placebo PO from Days 1 to 21 (given in 28-day cycles)

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

PO from Days 1 to 21 (given in 28-day cycles)

Number of subjects in period 1	Lenalidomide	Placebo
Started	29	17
Completed	0	0
Not completed	29	17
Adverse event, serious fatal	17	7
Consent withdrawn by subject	1	1
Adverse event, non-fatal	1	-

Progressive Disease	-	1
Study Terminated by Sponsor	10	8

Baseline characteristics

Reporting groups	
Reporting group title	Lenalidomide
Reporting group description:	
10mg/day PO from Days 1 to 21 (given in 28-day cycles)	
Reporting group title	Placebo
Reporting group description:	
Placebo PO from Days 1 to 21 (given in 28-day cycles)	

Reporting group values	Lenalidomide	Placebo	Total
Number of subjects	29	17	46
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	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	1	1
From 65-84 years	29	16	45
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	73.1	72.9	
standard deviation	± 4.41	± 6.77	-
Sex: Female, Male Units: Participants			
Female	8	5	13
Male	21	12	33
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	17	9	26
More than one race	0	0	0
Unknown or Not Reported	12	8	20
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	1	5
Not Hispanic or Latino	13	8	21
Unknown or Not Reported	12	8	20

End points

End points reporting groups

Reporting group title	Lenalidomide
Reporting group description:	
10mg/day PO from Days 1 to 21 (given in 28-day cycles)	
Reporting group title	Placebo
Reporting group description:	
Placebo PO from Days 1 to 21 (given in 28-day cycles)	

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)[1]
End point description:	
Overall Survival is defined as the time from the date of randomization to the date of death due to any cause.	
End point type	Primary
End point timeframe:	
Up to 76 months	
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: Only summary statistics planned for this endpoint	

End point values	Lenalidomide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	17		
Units: Months				
median (confidence interval 95%)	52.5 (39.1 to 99999)	99999 (30.1 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Participants with Adverse Events (AEs)

End point title	Incidence of Participants with Adverse Events (AEs)
End point description:	
Incidence of participants with adverse events (AEs) that measure type, frequency and severity of AEs graded by National Cancer Institute Common Terminology Criteria (NCI CTCAE V 4.0) including any grade adverse events (AEs), Grade 3-4 AEs, AEs related to study drug, grade 3-4 AEs related to study drug, any grade serious adverse events (SAEs), and SAEs related to study drug.	
End point type	Secondary
End point timeframe:	
From first dose to up to 28 days post last dose (Up to 44 months)	

End point values	Lenalidomide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	17		
Units: Participants				
Adverse Events (AEs)	29	15		
Grade 3-4 AEs	20	5		
AEs related to Study Drug	22	6		
Grade 3-4 AEs related to Study Drug	11	2		
Serious Adverse Events (SAEs)	15	4		
SAEs related to Study Drug	9	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Participants with Laboratory Abnormalities Shift from Baseline to Worst During Treatment

End point title	Incidence of Participants with Laboratory Abnormalities Shift from Baseline to Worst During Treatment

End point description:

Incidence of participants with laboratory abnormalities shift from baseline to worst during treatment in Hematology and Chemistry. Normal ranges will be used to determine the categories of high, low, and normal for lab tests that have no severity grade. low=participants with at least one value that was low relative to the normal range high=participants with at least one values that was high relative to the normal range both low and high=participants with at least one value that was low relative to the normal range and at least one value that was high relative to the normal range.

End point type	Secondary

End point timeframe:

Up to 44 months

End point values	Lenalidomide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	17		
Units: Participants				
Absolute neutrophils (Normal)	17	4		
Hemoglobin (Low)	1	0		
Hemoglobin (Normal)	10	2		
Platelets (Low)	1	1		
Platelets (Normal)	10	2		
White Blood Cell Count (Low)	2	0		
White Blood Cell Count (Normal)	14	4		
Corrected Serum Calcium (Normal)	11	3		
Corrected Serum Calcium (High)	1	0		
Creatinine Clearance (Normal)	11	2		

Creatinine Clearance (High)	1	0		
Serum Calcium (Low)	0	1		
Serum Calcium (Normal)	15	1		
Serum Creatinine (Low)	1	0		
Serum Creatinine (Normal)	11	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Participants with Vital Signs Abnormalities Shift from Baseline to Worst During Treatment

End point title	Incidence of Participants with Vital Signs Abnormalities Shift from Baseline to Worst During Treatment

End point description:

Incidence of participant with vital signs abnormalities shift from baseline to worst during treatment. Assessment is based on shift from normal and abnormal baseline categories. Normal range= ; 90 <= Systolic Blood pressure <= 120 (mmHg) ; 60 <= Diastolic Blood Pressure <= 80 (mmHg) ; 60 <= Pulse <= 100 (beats/min) ; 36.6 <= Temperature < 37.3 (°C)

End point type	Secondary

End point timeframe:

Up to 44 months

End point values	Lenalidomide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	17		
Units: Participants				
Diastolic Blood Pressure (Normal)	15	8		
Diastolic Blood Pressure (Abnormal)	2	0		
Systolic Blood Pressure (Normal)	9	3		
Systolic Blood Pressure (Abnormal)	1	0		
Pulse (Normal)	12	2		
Pulse (Abnormal)	1	0		
Temperature (Normal)	6	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Participants with Second Primary Malignancies (SPMs)

End point title	Incidence of Participants with Second Primary Malignancies (SPMs)

End point description:

Incidence of participants with second primary malignancies (SPMs) including all SPMs, Invasive SPMs (hematologic malignancies and solid tumors), and non-invasive SPMs (non-melanoma skin cancers).

End point type	Secondary

End point timeframe:

Up to 76 months

End point values	Lenalidomide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	17		
Units: Participants				
All SPMs	6	1		
Invasive SPMs	5	1		
Non-Invasive SPMs	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose to up to 28 days post last dose (Up to 44 months)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo PO from Days 1 to 21 (given in 28-day cycles) until documented progression disease	
Reporting group title	Lenalidomide
Reporting group description:	
10mg/day PO from Days 1 to 21 (given in 28-day cycles) until documented progression disease	

Serious adverse events	Placebo	Lenalidomide	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 17 (23.53%)	15 / 29 (51.72%)	
number of deaths (all causes)	8	17	
number of deaths resulting from adverse events			
Investigations			
General physical condition abnormal			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon neoplasm			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			

subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic bronchial carcinoma			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer metastatic			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

Deep vein thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin toxicity			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Pathological fracture			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Escherichia urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial prostatitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 29 (3.45%)	
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: 5 %

Non-serious adverse events	Placebo	Lenalidomide	
Total subjects affected by non-serious adverse events subjects affected / exposed	14 / 17 (82.35%)	27 / 29 (93.10%)	
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	1 / 17 (5.88%)	3 / 29 (10.34%)	
occurrences (all)	1	3	
Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	3 / 29 (10.34%)	
occurrences (all)	0	3	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 17 (17.65%)	5 / 29 (17.24%)	
occurrences (all)	4	7	
Asthenia			
subjects affected / exposed	0 / 17 (0.00%)	13 / 29 (44.83%)	
occurrences (all)	0	22	
Oedema peripheral			
subjects affected / exposed	1 / 17 (5.88%)	4 / 29 (13.79%)	
occurrences (all)	3	5	
Fatigue			
subjects affected / exposed	3 / 17 (17.65%)	3 / 29 (10.34%)	
occurrences (all)	4	3	
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 17 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	

Prostatitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Productive cough			
subjects affected / exposed	0 / 17 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Dyspnoea			
subjects affected / exposed	2 / 17 (11.76%)	2 / 29 (6.90%)	
occurrences (all)	2	4	
Cough			
subjects affected / exposed	5 / 17 (29.41%)	5 / 29 (17.24%)	
occurrences (all)	5	8	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 17 (5.88%)	2 / 29 (6.90%)	
occurrences (all)	1	3	
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
Blood creatinine increased			
subjects affected / exposed	1 / 17 (5.88%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
White blood cell count decreased			
subjects affected / exposed	1 / 17 (5.88%)	1 / 29 (3.45%)	
occurrences (all)	2	1	
Nervous system disorders			
Cervicobrachial syndrome			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	0 / 17 (0.00%)	4 / 29 (13.79%)	
occurrences (all)	0	4	
Paraesthesia			

subjects affected / exposed	2 / 17 (11.76%)	0 / 29 (0.00%)	
occurrences (all)	3	0	
Restless legs syndrome			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Sciatica			
subjects affected / exposed	0 / 17 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Somnolence			
subjects affected / exposed	1 / 17 (5.88%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 17 (11.76%)	3 / 29 (10.34%)	
occurrences (all)	4	4	
Neutropenia			
subjects affected / exposed	0 / 17 (0.00%)	11 / 29 (37.93%)	
occurrences (all)	0	27	
Thrombocytopenia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	4	
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 17 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	2	
Diverticulum			
subjects affected / exposed	2 / 17 (11.76%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
Dry mouth			
subjects affected / exposed	1 / 17 (5.88%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Enterocolitis			

subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 17 (5.88%)	8 / 29 (27.59%)	
occurrences (all)	1	10	
Abdominal pain upper			
subjects affected / exposed	1 / 17 (5.88%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Gastrointestinal angiectasia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	4 / 17 (23.53%)	7 / 29 (24.14%)	
occurrences (all)	6	19	
Vomiting			
subjects affected / exposed	1 / 17 (5.88%)	4 / 29 (13.79%)	
occurrences (all)	1	4	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 17 (0.00%)	3 / 29 (10.34%)	
occurrences (all)	0	3	
Rash			
subjects affected / exposed	0 / 17 (0.00%)	3 / 29 (10.34%)	
occurrences (all)	0	6	
Ingrowing nail			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	2 / 17 (11.76%)	3 / 29 (10.34%)	
occurrences (all)	5	4	
Erythema			
subjects affected / exposed	2 / 17 (11.76%)	2 / 29 (6.90%)	
occurrences (all)	2	2	
Diabetic foot			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences (all)	1	0	

Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 17 (5.88%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Pollakiuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 17 (11.76%)	2 / 29 (6.90%)	
occurrences (all)	2	3	
Bone pain			
subjects affected / exposed	4 / 17 (23.53%)	0 / 29 (0.00%)	
occurrences (all)	5	0	
Back pain			
subjects affected / exposed	3 / 17 (17.65%)	5 / 29 (17.24%)	
occurrences (all)	4	7	
Muscle contracture			
subjects affected / exposed	1 / 17 (5.88%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Muscle spasms			
subjects affected / exposed	2 / 17 (11.76%)	4 / 29 (13.79%)	
occurrences (all)	2	9	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 17 (11.76%)	0 / 29 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 17 (5.88%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
Myalgia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	1 / 17 (5.88%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Spinal pain			

subjects affected / exposed	2 / 17 (11.76%)	1 / 29 (3.45%)	
occurrences (all)	3	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 17 (11.76%)	8 / 29 (27.59%)	
occurrences (all)	4	13	
Conjunctivitis			
subjects affected / exposed	1 / 17 (5.88%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
Upper respiratory tract infection			
subjects affected / exposed	2 / 17 (11.76%)	4 / 29 (13.79%)	
occurrences (all)	2	4	
Pneumonia			
subjects affected / exposed	1 / 17 (5.88%)	4 / 29 (13.79%)	
occurrences (all)	1	5	
Influenza			
subjects affected / exposed	3 / 17 (17.65%)	6 / 29 (20.69%)	
occurrences (all)	3	6	
Nasopharyngitis			
subjects affected / exposed	1 / 17 (5.88%)	1 / 29 (3.45%)	
occurrences (all)	1	2	
Pharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	2 / 29 (6.90%)	
occurrences (all)	0	3	
Urinary tract infection			
subjects affected / exposed	1 / 17 (5.88%)	2 / 29 (6.90%)	
occurrences (all)	1	2	
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Hypercalcaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			

subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	2 / 29 (6.90%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 November 2013	Study Design Update
06 March 2014	Study Endpoints Update
31 October 2014	Exclusion and Inclusion Criteria Update
30 August 2015	Study Design Update
22 November 2017	Study Design and Endpoints Update

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported