Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Multiple Dose, Phase 2b Study to Demonstrate the Safety and Efficacy of Tildrakizumab in Subjects with Active Psoriatic Arthritis

Summary

EudraCT number	2016-003937-62
Trial protocol	HU ES PL
Global end of trial date	24 September 2019

Results information

Result version number	v1
This version publication date	29 October 2020
First version publication date	29 October 2020

Trial information

Trial identification

Sponsor protocol code	CLR_16_23

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02980692
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sun Pharma Global FZE
Sponsor organisation address	Office number 43 Bloc-Y, SAIF Zone, Sharjah, United Arab Emirates, 122304
Public contact	Head-Clinical Development, Sun Pharma Advanced Research Company Limited, +91 22 6645 5645, clinical.trials@sparcmail.com
Scientific contact	Head-Clinical Development, Sun Pharma Advanced Research Company Limited, +91 22 6645 5645, clinical.trials@sparcmail.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	Interim
Date of interim/final analysis	24 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 March 2019
Global end of trial reached?	Yes
Global end of trial date	24 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Parts 1 and 2
Primary Efficacy Objective
- To evaluate the optimal dose regimen of tildrakizumab in subjects with psoriatic arthritis (PsA) as measured by the proportion of subjects achieving a 20% reduction from Baseline in American College of Rheumatology response criteria [ACR20]) at Week 24.
Primary safety Objective (Parts 1 and 2):
- To assess the safety/tolerability and immunogenicity of multiple-dose administration of tildrakizumab in subjects with PsA.

Protection of trial subjects:

The trial and site activities were monitored according to the ICH-GCP guidelines considering every aspect of the trial, ensuring that the rights, safety and well-being of patients are protected and consistent with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 April 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 5
Country: Number of subjects enrolled	Mexico: 43
Country: Number of subjects enrolled	Russian Federation: 46
Country: Number of subjects enrolled	Ukraine: 40
Country: Number of subjects enrolled	United States: 73
Country: Number of subjects enrolled	Poland: 133
Country: Number of subjects enrolled	Spain: 38
Country: Number of subjects enrolled	Hungary: 13
Worldwide total number of subjects	391
EEA total number of subjects	184

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)	391
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

500 participants screened, 391 subjects randomized.

Period 1

Period 1 title	Double blind placebo controlled period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	SUNPG1623 I

Arm description:

Short-term dose

SUNPG1623 I: injection

Arm type	Experimental
Investigational medicinal product name	SUNPG1623 I
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

SUNPG1623 I administered by SC injection q4 weeks up until Week 48

Arm title	SUNPG1623 II

Arm description:

Mid-term dose

SUNPG1623 II: injection

PLACEBO: injection

Arm type	Experimental
Investigational medicinal product name	SUNPG1623 II
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

SUNPG1623 II administered SC q12 weeks up until Week 48

Arm title	SUNPG1623 dose III

Arm description:

Mid-term dose

SUNPG1623 III: injection

PLACEBO: injection

Arm type	Experimental

Investigational medicinal product name	SUNPG1623 dose III
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

SUNPG1623 dose III administered SC q12 weeks up until Week 48

Arm title	SUNPG1623 dose IV

Arm description:

Mid to long-term dose

SUNPG1623 IV: injection

PLACEBO: injection

Arm type	Experimental
Investigational medicinal product name	SUNPG1623 dose IV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

SUNPG1623 dose IV administered SC up until Week 48

Arm title	Placebo

Arm description:

Mid to long-term dose

PLACEBO: injection

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo administered SC up until Week 48

Number of subjects in period 1	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III
Started	78	79	77
Completed	69	73	65
Not completed	9	6	12
Consent withdrawn by subject	4	3	6
Physician decision	-	-	1
Others	1	-	-
Adverse event, non-fatal	-	2	-
Other	-	1	1
Lost to follow-up	3	-	4
Subject Died	1	-	-

Number of subjects in period 1	SUNPG1623 dose IV	Placebo
Started	78	79
Completed	69	68
Not completed	9	11
Consent withdrawn by subject	6	7
Physician decision	1	-
Others	-	-
Adverse event, non-fatal	-	1
Other	1	2
Lost to follow-up	1	1
Subject Died	-	-

Baseline characteristics

Reporting groups	
Reporting group title	SUNPG1623 I
Reporting group description: Short-term dose SUNPG1623 I: injection	
Reporting group title	SUNPG1623 II
Reporting group description: Mid-term dose SUNPG1623 II: injection PLACEBO: injection	
Reporting group title	SUNPG1623 dose III
Reporting group description: Mid-term dose SUNPG1623 III: injection PLACEBO: injection	
Reporting group title	SUNPG1623 dose IV
Reporting group description: Mid to long-term dose SUNPG1623 IV: injection PLACEBO: injection	
Reporting group title	Placebo
Reporting group description: Mid to long-term dose PLACEBO: injection	

Reporting group values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III
Number of subjects	78	79	77
Age categorical Units: Subjects			
Adults (18-64 years)	78	79	77
Age continuous Units: years			
arithmetic mean	50.1	49.3	49.2
standard deviation	± 13.28	± 11.24	± 11.85
Gender categorical Units: Subjects			
Female	46	37	47
Male	32	42	30

Reporting group values	SUNPG1623 dose IV	Placebo	Total
Number of subjects	78	79	391

Age categorical Units: Subjects			
Adults (18-64 years)	78	79	391
Age continuous Units: years			
arithmetic mean	47.2	48.1	
standard deviation	± 13.35	± 13.30	-
Gender categorical Units: Subjects			
Female	41	44	215
Male	37	35	176

End points

End points reporting groups

Reporting group title	SUNPG1623 I
Reporting group description: Short-term dose SUNPG1623 I: injection	

Reporting group title	SUNPG1623 II
Reporting group description: Mid-term dose SUNPG1623 II: injection PLACEBO: injection	

Reporting group title	SUNPG1623 dose III
Reporting group description: Mid-term dose SUNPG1623 III: injection PLACEBO: injection	

Reporting group title	SUNPG1623 dose IV
Reporting group description: Mid to long-term dose SUNPG1623 IV: injection PLACEBO: injection	

Reporting group title	Placebo
Reporting group description: Mid to long-term dose PLACEBO: injection	

Primary: Proportion of subjects who achieve ACR20 Response Criteria at Week 24

End point title	Proportion of subjects who achieve ACR20 Response Criteria at Week 24
End point description:	

End point type	Primary
End point timeframe: week 24	

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78	79	77	78
Units: percentage of response rate				
number (not applicable)	79.49	77.22	71.43	73.08

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: percentage of response rate				
number (not applicable)	50.63			

Statistical analyses

Statistical analysis title	Cochran-Mantel-Haenszel Analysis of ACR20 Response
Comparison groups	Placebo v SUNPG1623 I
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference (%)
Point estimate	28.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.84
upper limit	42.74
Variability estimate	Standard error of the mean
Dispersion value	7.12

Secondary: Proportion of Subjects Achieving ACR50 Response Criteria at Week 24

End point title	Proportion of Subjects Achieving ACR50 Response Criteria at Week 24
End point description:	
End point type	Secondary
End point timeframe:	
week 24	

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78	79	77	78
Units: percentage of response rate				
number (not applicable)	52.56	50.63	45.45	39.74

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: percentage of response rate				
number (not applicable)	24.05			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects Achieving ACR70 Response Criteria at Week 24

End point title	Proportion of Subjects Achieving ACR70 Response Criteria at Week 24

End point description:

End point type	Secondary

End point timeframe:

week 24

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78	79	77	78
Units: percentage of response rate				
number (not applicable)	28.21	29.11	22.08	16.67

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: percentage of response rate				
number (not applicable)	10.13			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Tender Joint Counts at Week 24

End point title	Change From Baseline in Tender Joint Counts at Week 24

End point description:

End point type	Secondary

End point timeframe:

week 24

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	78	76	78
Units: Change from Baseline				
least squares mean (standard error)	-11.9 (± 1.04)	-12.6 (± 1.01)	-12.9 (± 1.03)	-12.0 (± 1.04)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: Change from Baseline				
least squares mean (standard error)	-9.4 (± 1.02)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Swollen Joint Counts at Week 24

End point title	Change from Baseline in Swollen Joint Counts at Week 24

End point description:

End point type	Secondary

End point timeframe:

24 weeks

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	78	76	78
Units: Change From Baseline				
least squares mean (standard error)	-8.3 (± 0.52)	-7.7 (± 0.51)	-8.2 (± 0.52)	-7.6 (± 0.52)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: Change From Baseline				
least squares mean (standard error)	-6.5 (± 0.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Physician Global Assessment of Disease Activity VAS at Week 24

End point title	Physician Global Assessment of Disease Activity VAS at Week 24

End point description:

End point type	Secondary

End point timeframe:

24 weeks

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	78	76	78
Units: change from baseline				
least squares mean (standard error)	-36.5 (± 2.15)	-38.8 (± 2.08)	-37.5 (± 2.11)	-36.3 (± 2.14)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: change from baseline				
least squares mean (standard error)	-23.5 (± 2.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Health Assessment Questionnaire- Disability Index at Week 24

End point title	Health Assessment Questionnaire- Disability Index at Week 24

End point description:

End point type	Secondary

End point timeframe:

24 weeks

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	78	76	78
Units: Change From Baseline in HAQ-DI				
least squares mean (standard error)	-0.3013 (± 0.05196)	-0.3314 (± 0.05054)	-0.3337 (± 0.05128)	-0.2376 (± 0.05187)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: Change From Baseline in HAQ-DI				
least squares mean (standard error)	-0.1827 (± 0.05102)			

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects Requiring Adjustment of Background Therapy at Week 16

End point title	Subjects Requiring Adjustment of Background Therapy at Week 16

End point description:

End point type	Secondary

End point timeframe:

24 weeks

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78	79	77	78
Units: percentage				
number (confidence interval 95%)	0.00 (0.00 to 0.00)	1.27 (0.00 to 3.73)	1.30 (0.00 to 3.83)	2.56 (0.00 to 6.07)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: percentage				
number (confidence interval 95%)	1.27 (0.00 to 3.73)			

Statistical analyses

No statistical analyses for this end point

Secondary: Minimal Disease Activity at Week 24

End point title	Minimal Disease Activity at Week 24

End point description:

End point type	Secondary

End point timeframe:

24 weeks

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78	79	77	78
Units: percentage response rate				
number (not applicable)	33.33	34.18	28.57	19.23

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: percentage response rate				
number (not applicable)	6.33			

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's Pain Assessment up to Week 24

End point title	Patient's Pain Assessment up to Week 24

End point description:

End point type	Secondary

End point timeframe:
week 24

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	78	76	78
Units: units				
least squares mean (standard error)	-35.1 (± 2.69)	-31.6 (± 2.60)	-32.1 (± 2.64)	-28.8 (± 2.68)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: units				
least squares mean (standard error)	-21.5 (± 2.63)			

Statistical analyses

No statistical analyses for this end point

Secondary: Acute Phase C - Reactive Protein at Week 24

End point title	Acute Phase C - Reactive Protein at Week 24

End point description:

End point type	Secondary

End point timeframe:
week 24

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	78	76	78
Units: units				
least squares mean (standard error)	-3.56 (± 1.088)	-2.33 (± 1.054)	-3.23 (± 1.071)	-2.06 (± 1.088)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: units				
least squares mean (standard error)	0.55 (± 1.065)			

Statistical analyses

No statistical analyses for this end point

Secondary: Erythrocyte Sedimentation Rate at Week 24

End point title	Erythrocyte Sedimentation Rate at Week 24

End point description:

End point type	Secondary

End point timeframe:

week 24

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	69	68
Units: units				
least squares mean (standard error)	-8.0 (± 1.86)	-6.9 (± 1.85)	-8.2 (± 1.84)	-8.7 (± 1.89)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: units				
least squares mean (standard error)	-2.3 (± 1.95)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Leeds Dactylitis Index (LDI) at Week 24

End point title	Change from Baseline in Leeds Dactylitis Index (LDI) at Week 24

End point description:

End point type	Secondary

End point timeframe:

week 24

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	56	46	48
Units: units				
least squares mean (standard error)	-22.987 (± 3.5112)	-25.123 (± 3.2307)	-27.572 (± 3.5088)	-19.873 (± 3.4520)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: units				
least squares mean (standard error)	-24.706 (± 3.2252)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Leeds Enthesitis Index (LEI) at Week 24

End point title	Change from Baseline in Leeds Enthesitis Index (LEI) at Week 24

End point description:

End point type	Secondary

End point timeframe:
week 24

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	77	75	76
Units: units				
least squares mean (standard error)	-1.3 (± 0.16)	-0.9 (± 0.15)	-1.2 (± 0.15)	-1.1 (± 0.15)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	78			
Units: units				
least squares mean (standard error)	-0.8 (± 0.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Patient’s Global Assessment of Disease Activity at Week 24

End point title	Patient’s Global Assessment of Disease Activity at Week 24

End point description:

End point type	Secondary

End point timeframe:
week 24

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	78	76	78
Units: units				
least squares mean (standard error)	-35.0 (± 2.60)	-33.3 (± 2.52)	-33.4 (± 2.56)	-30.4 (± 2.60)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	79			

Units: units				
least squares mean (standard error)	-21.7 (± 2.54)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Activity Score (DAS) 28 (joints) C - reactive protein (DAS28-CRP) response rate at Week 24

End point title	Disease Activity Score (DAS) 28 (joints) C - reactive protein (DAS28-CRP) response rate at Week 24

End point description:

End point type	Secondary

End point timeframe:

week 24

End point values	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III	SUNPG1623 dose IV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78	79	77	78
Units: response rate (%)				
number (not applicable)	58.97	64.56	58.44	53.85

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: response rate (%)				
number (not applicable)	30.38			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 52 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	SUNPG1623 I
Reporting group description: Short-term dose SUNPG1623 I: injection	
Reporting group title	SUNPG1623 II
Reporting group description: Mid-term dose SUNPG1623 II: injection PLACEBO: injection	
Reporting group title	SUNPG1623 dose III
Reporting group description: Mid-term dose SUNPG1623 III: injection PLACEBO: injection	
Reporting group title	SUNPG1623 dose IV
Reporting group description: Mid to long-term dose SUNPG1623 IV: injection PLACEBO: injection	
Reporting group title	Placebo
Reporting group description: Mid to long-term dose PLACEBO: injection	

Serious adverse events	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intraductal proliferative breast lesion			

subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parathyroid tumour benign			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
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			
Ankle fracture			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Lumbar radiculopathy			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple sclerosis			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst ruptured			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			

subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
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			
Bronchitis			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic tonsillitis			

subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pnemonia			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	5 / 78 (6.41%)	3 / 79 (3.80%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	SUNPG1623 dose IV	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intraductal proliferative breast lesion			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parathyroid tumour benign			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
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			
Ankle fracture			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			

subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Lumbar radiculopathy			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst ruptured			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			

subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic tonsillitis			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pnemonia			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	4 / 78 (5.13%)	5 / 79 (6.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	SUNPG1623 I	SUNPG1623 II	SUNPG1623 dose III
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 78 (2.56%)	0 / 79 (0.00%)	1 / 77 (1.30%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intraductal proliferative breast lesion			
subjects affected / exposed	2 / 78 (2.56%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 78 (2.56%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Pleurisy			
subjects affected / exposed	2 / 78 (2.56%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	0
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 78 (2.56%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	0
Pyelonephritis			
subjects affected / exposed	2 / 78 (2.56%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	2 / 78 (2.56%)	0 / 79 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1

Non-serious adverse events	SUNPG1623 dose IV	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 78 (1.28%)	1 / 79 (1.27%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intraductal proliferative breast lesion			
subjects affected / exposed	1 / 78 (1.28%)	1 / 79 (1.27%)	
occurrences (all)	1	0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 78 (1.28%)	1 / 79 (1.27%)	
occurrences (all)	0	1	

Respiratory, thoracic and mediastinal disorders			
Pleurisy			
subjects affected / exposed	1 / 78 (1.28%)	1 / 79 (1.27%)	
occurrences (all)	0	0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 78 (1.28%)	1 / 79 (1.27%)	
occurrences (all)	0	0	
Pyelonephritis			
subjects affected / exposed	1 / 78 (1.28%)	1 / 79 (1.27%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	1 / 78 (1.28%)	1 / 79 (1.27%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 March 2018	The revisions are summarized as follows. • Addition of reference to LTE study throughout. • Correction of text describing definition of minimal response. • Addition of text describing requirements for subjects taking low-potency opioids. • Clarification of use of topical corticosteroids. • Clarification that measurement of height was only required once, at Screening. • Addition of text clarifying visits requiring measurement of BSA. • Change of protocol version number and date. • Correction of minor typographical errors throughout.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported