

**Clinical trial results:****A Randomized, Double-Blind, Placebo-Controlled Phase 2a Study to Evaluate the Efficacy and Safety of Tildrakizumab in Subjects with Active Ankylosing Spondylitis or Non-Radiographic Axial Spondyloarthritis****Summary**

EudraCT number	2016-003936-19
Trial protocol	HU ES
Global end of trial date	03 September 2019

Results information

Result version number	v1 (current)
This version publication date	19 December 2020
First version publication date	19 December 2020

Trial information**Trial identification**

Sponsor protocol code	CLR_16_22
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Sun Pharma Global FZE
Sponsor organisation address	#43, Block Y, SAIF Zone, Sharjah, United Arab Emirates, 122304
Public contact	Shravanti Bhowmik, MD, Sun Pharmaceuticals Advanced Research Company Limited, +91 22 6645 5645, shravanti.bhowmik@sparcmail.com
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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	03 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 February 2019
Global end of trial reached?	Yes
Global end of trial date	03 September 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary Efficacy Objective (Part 1)

- To evaluate the efficacy of tildrakizumab in subjects with AS or nr-axSpA, as measured by the proportion of subjects achieving Assessment of SpondyloArthritis international Society (ASAS) criteria defined as $\geq 20\%$ improvement in 3 of 4 assessment domains (ASAS20) response criteria 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 AS or nr-axSpA.

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	07 February 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	Poland: 87
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	101
EEA total number of subjects	96

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)	101
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

101 subjects with active AS were enrolled and randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	SUNPG1622 I
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Arm description:

SUNPG1622 I dose: Injection

Arm type	Experimental
Investigational medicinal product name	SUNPG1622 I
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

SUNPG1622 I administered by Subcutaneous injections, every 4 weeks

Arm title	Placebo
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Arm description:

Placebo: Injection

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo administered SC injection every 4 weeks

Number of subjects in period 1	SUNPG1622 I	Placebo
Started	50	51
Completed	42	40
Not completed	8	11
Consent withdrawn by subject	-	1
Adverse event, non-fatal	-	1

Withdrawal by Subject	6	9
Lost to follow-up	2	-

Baseline characteristics

Reporting groups

Reporting group title	Overall Study (overall period)
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Reporting group description: -

Reporting group values	Overall Study (overall period)	Total	
Number of subjects	101	101	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	39.5 ± 10.10	-	
Gender categorical Units: Subjects			
Female	24	24	
Male	77	77	

End points

End points reporting groups

Reporting group title	SUNPG1622 I
Reporting group description:	SUNPG1622 I dose: Injection
Reporting group title	Placebo
Reporting group description:	Placebo: Injection

Primary: Assessment of SpondyloArthritis International Society 20 Response Rates at Week 24

End point title	Assessment of SpondyloArthritis International Society 20 Response Rates at Week 24
End point description:	
End point type	Primary
End point timeframe:	Week 24

End point values	SUNPG1622 I	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	51		
Units: Number				
number (confidence interval 95%)	74.00 (61.84 to 86.16)	83.67 (73.32 to 94.02)		

Statistical analyses

Statistical analysis title	Cochran-Mantel-Haenszel Analysis-ASAS20 Response
Comparison groups	SUNPG1622 I v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4439
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference (%)
Point estimate	-6.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.34
upper limit	9.71

Variability estimate	Standard error of the mean
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Secondary: Assessment of SpondyloArthritis International Society 20 Response Rates up to Week 24

End point title	Assessment of SpondyloArthritis International Society 20 Response Rates up to Week 24
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End point description:

End point type	Secondary
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End point timeframe:
Week 24

End point values	SUNPG1622 I	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	49		
Units: Number				
number (confidence interval 95%)	74.00 (61.84 to 86.16)	83.67 (73.32 to 94.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of SpondyloArthritis International Society 20 Response Rates

End point title	Assessment of SpondyloArthritis International Society 20 Response Rates
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End point description:

End point type	Secondary
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End point timeframe:
Week 52

End point values	SUNPG1622 I	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	47		
Units: number				
number (confidence interval 95%)	88.89 (78.62 to 99.15)	76.60 (64.49 to 88.70)		

Statistical analyses

No statistical analyses for this end point

Secondary: The percentage of subjects who required adjustment of background therapy at Week 16 for the FAS

End point title	The percentage of subjects who required adjustment of background therapy at Week 16 for the FAS
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End point description:

End point type	Secondary
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End point timeframe:

Week 16

End point values	SUNPG1622 I	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	51		
Units: number				
number (confidence interval 95%)	2 (0.00 to 9.43)	0 (0.00 to 9.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: The percentage of subjects who required adjustment of background therapy for the PPAS

End point title	The percentage of subjects who required adjustment of background therapy for the PPAS
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End point description:

End point type	Secondary
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End point timeframe:

Week 16

End point values	SUNPG1622 I	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	44		
Units: number				
number (confidence interval 95%)	1 (0.00 to 6.12)	0 (0.00 to 6.12)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Assessment of SpondyloArthritis International Society 70 Response Rates at Measured Time Points

End point title	Assessment of SpondyloArthritis International Society 70 Response Rates at Measured Time Points			
End point description:				
End point type	Other pre-specified			
End point timeframe:	Week 72			

End point values	SUNPG1622 I	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	51		
Units: number				
number (confidence interval 95%)	33.33 (19.08 to 47.59)	31.71 (17.46 to 45.95)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Assessment of SpondyloArthritis International Society Response Rates 5/6 at Measured Time Points

End point title	Assessment of SpondyloArthritis International Society Response Rates 5/6 at Measured Time Points			
End point description:				
End point type	Other pre-specified			
End point timeframe:	Week 72			

End point values	SUNPG1622 I	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	41		
Units: number				
number (confidence interval 95%)	52.38 (37.28 to 67.49)	39.02 (24.09 to 53.96)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Week 72

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	Part 1: SUNPG1622 or Placebo
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Reporting group description: -

Reporting group title	Part 2: Treatment Follow-up (SUNPG16221 Dose Injection)
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Reporting group description: -

Reporting group title	Part 3: Washout
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Reporting group description: -

Serious adverse events	Part 1: SUNPG1622 or Placebo	Part 2: Treatment Follow-up (SUNPG16221 Dose Injection)	Part 3: Washout
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	1 / 101 (0.99%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroadenoma of breast			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	1 / 101 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperplasia			

subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	0 / 101 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0.5 %

Non-serious adverse events	Part 1: SUNPG1622 or Placebo	Part 2: Treatment Follow-up (SUNPG16221 Dose Injection)	Part 3: Washout
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 101 (11.88%)	10 / 101 (9.90%)	0 / 101 (0.00%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	0 / 101 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	0 / 101 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	0 / 101 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	0 / 101 (0.00%)
occurrences (all)	1	0	0
Weight increased			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	0 / 101 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Blood pressure increased			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	0 / 101 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Hyperplasia			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	0 / 101 (0.00%)
occurrences (all)	0	1	0

Injection site erythema subjects affected / exposed occurrences (all)	0 / 101 (0.00%) 0	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0
Injection site joint erythema subjects affected / exposed occurrences (all)	0 / 101 (0.00%) 0	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0
Skin and subcutaneous tissue disorders			
Dermatitis allergic subjects affected / exposed occurrences (all)	1 / 101 (0.99%) 1	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0
Erythema subjects affected / exposed occurrences (all)	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0	0 / 101 (0.00%) 0
Endocrine disorders			
Glucose tolerance impaired subjects affected / exposed occurrences (all)	0 / 101 (0.00%) 0	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	0 / 101 (0.00%) 0	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0
Herpes simplex subjects affected / exposed occurrences (all)	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0	0 / 101 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0	0 / 101 (0.00%) 0
Sinusitis subjects affected / exposed occurrences (all)	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0	0 / 101 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0	0 / 101 (0.00%) 0
Vaginal infection subjects affected / exposed occurrences (all)	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0	0 / 101 (0.00%) 0
Metabolism and nutrition disorders			

Blood glucose increased subjects affected / exposed occurrences (all)	0 / 101 (0.00%) 0	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0
Dyslipidaemia subjects affected / exposed occurrences (all)	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0	0 / 101 (0.00%) 0
Hypercholesterolaemia subjects affected / exposed occurrences (all)	0 / 101 (0.00%) 0	1 / 101 (0.99%) 1	0 / 101 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 June 2017	<ol style="list-style-type: none">1. Allowance of subjects who failed to meet minimal response criteria at Week 16 to continue in Part 1 and 2 of the study, with the possibility for adjustment of background therapy at Week 16.2. Amendment of primary and secondary endpoints to improve characteristics for the power of the study.3. Revision of ASAS20, ASAS40, and ASAS70 definitions for clarification.4. Addition of exclusion criteria regarding bilateral sacroiliac joint fusion and fused discovertebral units.5. Addition of definition of stable dose for NSAIDs.7. Addition of 2 stages to study to prioritize the development program for AS and nr-axSpA.8. Addition of requirement that any non-drug therapy was stable for 4 weeks prior to IMP initiation.
19 March 2018	<ol style="list-style-type: none">1. Added reference to LTE study throughout.2. Correction of text describing the definition of minimal response.3. Addition of text describing requirements for subjects taking low-potency opioids.4. Clarification that measurement of height was only required once, at Screening.5. Addition of high sensitivity CRP collection at Screening for subjects with non-radiographic axial spondyloarthritis.6. Editorial and administrative changes implemented throughout the document.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported