Clinical trial results:
A 52-week, multicenter study to assess the time course of response to secukinumab on joint inflammation using Power Doppler ultrasonography in patients with active psoriatic arthritis.

Summary

EudraCT number	2015-002394-38
Trial protocol	GB IE ES HU BE NO FR AT NL CZ DE IT
Global end of trial date	10 November 2020

Results information

Result version number	v1 (current)
This version publication date	25 November 2021
First version publication date	25 November 2021

Trial information

Trial identification

Sponsor protocol code	CAIN457F2354

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02662985
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharma AG, 1 8627788300, novartis.email@novartis.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	10 November 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that there is a difference between secukinumab and placebo in terms of joint synovitis response over 12 weeks as measured by the PDUS Global EULAR-OMERACT-Synovitis Score (GLOESS) of the affected joints (out of 48 joints) in PsA patients with an inadequate response to non-biologic DMARDs.

Protection of trial subjects:

This study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 August 2016
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: 18
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Colombia: 1
Country: Number of subjects enrolled	Czechia: 19
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Mexico: 49
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 5

Worldwide total number of subjects	166
EEA total number of subjects	89

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)	155
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

166 participants enrolled in 17 countries

Pre-assignment

Screening details:

83 partcipants were randomized to each group

Period 1

Period 1 title	Treatment Period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 - Secukinumab (150 mg + 300 mg)

Arm description:

In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to the severity of skin PSO disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment at the same previous dose up to Week 52

Arm type	Experimental
Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

150 mg and 300 mg s.c.

Arm title	Group 2 - Placebo

Arm description:

In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg according to the severity of skin PSO disease 150 mg for mild PSO and 300 mg for moderate to severe PSO every 4 weeks from Week 12, as follows, based on their severity of skin disease at Week 12 In Treatment Period-3: Continue wih the same dose of secukinumab 150 mg or 300 mg open-label

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

Dosage and administration details:

150 mg and 300 mg s.c.

Number of subjects in period 1	Group 1 - Secukinumab (150 mg + 300 mg)	Group 2 - Placebo
Started	83	83
Completed	82	79
Not completed	1	4
Physician decision	1	-
Consent withdrawn by subject	-	1
Adverse event, non-fatal	-	2
Protocol deviation	-	1

Period 2

Period 2 title	Treatment period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 - Secukinumab (150 mg + 300 mg)

Arm description:

In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to severity of skin disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same active dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment up to Week 52

Arm type	Experimental
Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

150 mg and 300 mg s.c.

Arm title	Group 2 - Placebo/secukinumab

Arm description:

In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg every 4 weeks from Week 12, as follows, based on severity of skin psoriasis at Week 12 In Treatment Period-3: Continued with the same dose of secukinumab 150 mg or 300 mg open label.

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

Dosage and administration details:

150 mg and 300 mg s.c.

Number of subjects in period 2	Group 1 - Secukinumab (150 mg + 300 mg)	Group 2 - Placebo/secukinumab
Started	82	79
Completed	81	78
Not completed	1	1
Lost to follow-up	1	-
Lack of efficacy	-	1

Period 3

Period 3 title	Treatment period 3 (extension period)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 - Secukinumab (150 mg + 300 mg)

Arm description:

In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to the severity of skin disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same active dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment at the same dose up to Week 52

Arm type	Experimental
Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

150 mg and 300 mg s.c.

Arm title	Group 2 - Placebo/secukinumab

Arm description:

In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg according to severity of skin PSO 150 mg for mild PSO and 300 mg for moderate to severe skin PSO every 4

weeks from Week 12, as follows, based on severity of skin psoriasis at Week 12 In Treatment Period-3: Open-label secukinumab at the same dose continued to be assigned to patients

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

Dosage and administration details:

150 mg and 300 mg s.c.

Number of subjects in period 3	Group 1 - Secukinumab (150 mg + 300 mg)	Group 2 - Placebo/secukinumab
Started	81	78
Completed	75	69
Not completed	6	9
Adverse event, serious fatal	-	1
Consent withdrawn by subject	1	2
Withdrew before entering period	4	4
Adverse event, non-fatal	1	1
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Group 1 - Secukinumab (150 mg + 300 mg)
Reporting group description:	
In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to the severity of skin PSO disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment at the same previous dose up to Week 52	
Reporting group title	Group 2 - Placebo
Reporting group description:	
In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg according to the severity of skin PSO disease 150 mg for mild PSO and 300 mg for moderate to severe PSO every 4 weeks from Week 12, as follows, based on their severity of skin disease at Week 12 In Treatment Period-3: Continue wih the same dose of secukinumab 150 mg or 300 mg open-label	

Reporting group values	Group 1 - Secukinumab (150 mg + 300 mg)	Group 2 - Placebo	Total
Number of subjects	83	83	166
Age Categorical Units:			
<=18 years	0	0	0
Between 18 and 65 years	76	79	155
>=65 years	7	4	11
Age Continuous Units: years			
arithmetic mean	46.7	46.7	
standard deviation	± 12.35	± 12.08	-
Sex: Female, Male Units:			
Female	45	46	91
Male	38	37	75
Race/Ethnicity, Customized Units: Subjects			
Caucasian	75	75	150
Asian	1	0	1
Native American	4	8	12
Unknown	2	0	2
Other	1	0	1

End points

End points reporting groups

Reporting group title	Group 1 - Secukinumab (150 mg + 300 mg)

Reporting group description:

In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to the severity of skin PSO disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment at the same previous dose up to Week 52

Reporting group title	Group 2 - Placebo

Reporting group description:

In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg according to the severity of skin PSO disease 150 mg for mild PSO and 300 mg for moderate to severe PSO every 4 weeks from Week 12, as follows, based on their severity of skin disease at Week 12 In Treatment Period-3: Continue wih the same dose of secukinumab 150 mg or 300 mg open-label

Reporting group title	Group 1 - Secukinumab (150 mg + 300 mg)

Reporting group description:

In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to severity of skin disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same active dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment up to Week 52

Reporting group title	Group 2 - Placebo/secukinumab

Reporting group description:

In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg every 4 weeks from Week 12, as follows, based on severity of skin psoriasis at Week 12 In Treatment Period-3: Continued with the same dose of secukinumab 150 mg or 300 mg open label.

Reporting group title	Group 1 - Secukinumab (150 mg + 300 mg)

Reporting group description:

In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to the severity of skin disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same active dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment at the same dose up to Week 52

Reporting group title	Group 2 - Placebo/secukinumab

Reporting group description:

In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg according to severity of skin PSO 150 mg for mild PSO and 300 mg for moderate to severe skin PSO every 4 weeks from Week 12, as follows, based on severity of skin psoriasis at Week 12 In Treatment Period-3: Open-label secukinumab at the same dose continued to be assigned to patients

Primary: Difference between secukinumab and placebo in terms of joint synovitis as measured by the Power Doppler Ultrasonography (PDUS) Global OMERACT-EULAR Synovitis Score (GLOESS)

End point title	Difference between secukinumab and placebo in terms of joint synovitis as measured by the Power Doppler Ultrasonography (PDUS) Global OMERACT-EULAR Synovitis Score (GLOESS)

End point description:

Mixed model repeated measures (MMRM) analysis of change in Global OMERACT-EULAR Synovitis Score (GLOESS) score at Week 12 (observed data) to compare treatments.

GLOESS score can vary from 0 to 144 with highest rating reflecting higher severity.

End point type	Primary

End point timeframe:

12 weeks

End point values	Group 1 - Secukinumab (150 mg + 300 mg)	Group 2 - Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	81		
Units: Adjusted Mean Change in scores				
arithmetic mean (standard error)	-9.05 (± 0.94)	-5.86 (± 0.93)		

Statistical analyses

Statistical analysis title	PDUS GLOESS score

Statistical analysis description:

GLOESS scores

Comparison groups	Group 2 - Placebo v Group 1 - Secukinumab (150 mg + 300 mg)
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	Adjusted Mean Difference
Point estimate	-3.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.52
upper limit	-0.85
Variability estimate	Standard error of the mean
Dispersion value	1.18

Secondary: Proportion of Participants with American College of Rheumatology (ACR)-20 response - Key Secondary

End point title	Proportion of Participants with American College of Rheumatology (ACR)-20 response - Key Secondary

End point description:

Key Secondary Outcome: ACR 20 responder has ≥ 20% improvement in TJC and SJC and >20% improvement in 3 of the following 5 domains: patient’s assessment of disease activity, physician’s assessment of disease activity, patient’s assessment of PsA pain, HAQ-DI, or hsCRP.

End point type	Secondary

End point timeframe:

Week 12

End point values	Group 1 - Secukinumab (150 mg + 300 mg)	Group 2 - Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	83		
Units: participants	56	26		

Statistical analyses

Statistical analysis title	ACR-20
Statistical analysis description:	
Proportion of patients with ACR 20 response at Week 12 (FAS)	
Comparison groups	Group 1 - Secukinumab (150 mg + 300 mg) v Group 2 - Placebo
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.38
upper limit	8.89

Secondary: Proportion of Participants with American College of Rheumatology (ACR)-50 response - Key Secondary

End point title	Proportion of Participants with American College of Rheumatology (ACR)-50 response - Key Secondary
End point description:	
ACR 50 responder has ≥ 50% improvement in TJC and SJC and >25% improvement in 3 of the following 5 domains: patient’s assessment of disease activity, physician’s assessment of disease activity, patient’s assessment of PsA pain, HAQ-DI, or hsCRP.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	Group 1 - Secukinumab (150 mg + 300 mg)	Group 2 - Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	83		
Units: participants	38	7		

Statistical analyses

Statistical analysis title	ACR-50
Statistical analysis description:	
Proportion of patients with ACR 50 response at Week 12 (FAS)	
Comparison groups	Group 1 - Secukinumab (150 mg + 300 mg) v Group 2 - Placebo
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	9.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.92
upper limit	23.75

Secondary: Spondyloarthritis Research Consortium of Canada (SPARCC) - Key Secondary

End point title	Spondyloarthritis Research Consortium of Canada (SPARCC) - Key Secondary
End point description:	
Repeated measures mixed effect (MMRM) analysis of SPARCC total score change from baseline to Week 12 between the 2 treatment groups. SPARCC index ranges from 0 to 16.	
End point type	Secondary
End point timeframe:	
Baseline to Week 12	

End point values	Group 1 - Secukinumab (150 mg + 300 mg)	Group 2 - Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	81		
Units: Adjusted mean change in scores				
arithmetic mean (standard error)	-2.23 (± 0.29)	-1.57 (± 0.29)		

Statistical analyses

Statistical analysis title	SPARCC
Statistical analysis description: SPARCC total score change	
Comparison groups	Group 1 - Secukinumab (150 mg + 300 mg) v Group 2 - Placebo
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0327
Method	Mixed models analysis
Parameter estimate	Adjusted Mean Difference
Point estimate	-0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.374
upper limit	0.043

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected for the maximum duration of treatment and follow up for a participant per protocol for 12 weeks. All cause mortality (deaths) was collected from FPFV to LPLV up to a maximum of 52 weeks

Adverse event reporting additional description:

Adverse Events (AEs) are any untoward sign or symptom that occurs during the study treatment period with a frequency greater than or equal to 2%

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Secukinumab (150+300 mg)

Reporting group description:

Secukinumab (150+300 mg)

Reporting group title	Placebo

Reporting group description:

Placebo

Serious adverse events	Secukinumab (150+300 mg)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 161 (5.59%)	2 / 83 (2.41%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 161 (0.62%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			
subjects affected / exposed	1 / 161 (0.62%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			

subjects affected / exposed	1 / 161 (0.62%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 161 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	1 / 161 (0.62%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 161 (1.24%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 161 (0.62%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	1 / 161 (0.62%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 161 (0.00%)	1 / 83 (1.20%)	
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	1 / 161 (0.62%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	1 / 161 (0.62%)	0 / 83 (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			
COVID-19			
subjects affected / exposed	1 / 161 (0.62%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
Malnutrition			
subjects affected / exposed	1 / 161 (0.62%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Secukinumab (150+300 mg)	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 161 (49.07%)	27 / 83 (32.53%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 161 (0.62%)	2 / 83 (2.41%)	
occurrences (all)	1	3	
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 161 (5.59%)	1 / 83 (1.20%)	
occurrences (all)	11	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 161 (1.24%)	2 / 83 (2.41%)	
occurrences (all)	2	2	

Headache			
subjects affected / exposed	13 / 161 (8.07%)	3 / 83 (3.61%)	
occurrences (all)	18	3	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 161 (2.48%)	1 / 83 (1.20%)	
occurrences (all)	4	1	
Fatigue			
subjects affected / exposed	4 / 161 (2.48%)	0 / 83 (0.00%)	
occurrences (all)	4	0	
Eye disorders			
Dry eye			
subjects affected / exposed	3 / 161 (1.86%)	3 / 83 (3.61%)	
occurrences (all)	3	3	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 161 (3.11%)	3 / 83 (3.61%)	
occurrences (all)	5	3	
Constipation			
subjects affected / exposed	4 / 161 (2.48%)	1 / 83 (1.20%)	
occurrences (all)	4	1	
Diarrhoea			
subjects affected / exposed	7 / 161 (4.35%)	6 / 83 (7.23%)	
occurrences (all)	9	6	
Nausea			
subjects affected / exposed	4 / 161 (2.48%)	1 / 83 (1.20%)	
occurrences (all)	4	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 161 (5.59%)	2 / 83 (2.41%)	
occurrences (all)	10	2	
Productive cough			
subjects affected / exposed	0 / 161 (0.00%)	2 / 83 (2.41%)	
occurrences (all)	0	2	
Rhinorrhoea			

subjects affected / exposed	2 / 161 (1.24%)	2 / 83 (2.41%)	
occurrences (all)	2	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 161 (1.86%)	3 / 83 (3.61%)	
occurrences (all)	3	4	
Back pain			
subjects affected / exposed	4 / 161 (2.48%)	2 / 83 (2.41%)	
occurrences (all)	4	2	
Infections and infestations			
Bronchitis			
subjects affected / exposed	8 / 161 (4.97%)	2 / 83 (2.41%)	
occurrences (all)	9	2	
Gastroenteritis			
subjects affected / exposed	4 / 161 (2.48%)	1 / 83 (1.20%)	
occurrences (all)	4	1	
Influenza			
subjects affected / exposed	7 / 161 (4.35%)	3 / 83 (3.61%)	
occurrences (all)	7	4	
Nasopharyngitis			
subjects affected / exposed	19 / 161 (11.80%)	4 / 83 (4.82%)	
occurrences (all)	26	5	
Oral herpes			
subjects affected / exposed	4 / 161 (2.48%)	1 / 83 (1.20%)	
occurrences (all)	6	1	
Pharyngitis			
subjects affected / exposed	5 / 161 (3.11%)	0 / 83 (0.00%)	
occurrences (all)	5	0	
Upper respiratory tract infection			
subjects affected / exposed	4 / 161 (2.48%)	2 / 83 (2.41%)	
occurrences (all)	4	2	
Urinary tract infection			
subjects affected / exposed	10 / 161 (6.21%)	3 / 83 (3.61%)	
occurrences (all)	10	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 June 2016	For those countries where it was required, hepatitis B, hepatitis C and human immunodeficiency virus (HIV) serology testing during the Screening Period were added to the assessment schedule. These tests were already outlined in Exclusion Criterion No. 21 and results of these tests determined eligibility for the study. Thus the addition to the assessment schedule in this amendment was made in order to clarify and remove inconsistencies in the protocol. Collection of SPARCC at the Screening Visit was added to the assessment schedule as it was previously omitted in error. This test was already outlined in Inclusion Criterion No.5 and results of this test determined eligibility for the study. Thus the addition to the assessment schedule in this amendment was made in order to clarify and remove inconsistencies in the protocol.
02 March 2017	1. To increase the study feasibility and to ease the study visit burden on patients without compromising the primary and secondary objectives of the study until Week 12. Inclusion criterion no. 4, an ultrasound entry criterion that was considered too restrictive as it resulted in the most screen failures, was amended to allow inclusion of patients with a total synovitis score ≥ 2 and inflammation related to PD signal ≥ 2 for at least 1 affected joint as observed via PDUS of 48 joints, OR with an inflammation related to PD signal ≥ 1 for at least 2 affected joints as observed via PDUS of 48 joints. The study visits and associated study assessments at Week 28, 32, 40, 44 and 48 were removed from the open-label Extension Period and home administration of study drug was introduced at these time points. The clinical efficacy assessments (including PDUS assessments) were removed from the double-blind Week 3 visit; and the PDUS assessment was removed from the Week 56 follow-up visit. The Extension Period was optional according to Investigator’s judgment and patient consent and exploratory study objectives only applied to this period. The removal of study visits during the Extension Period did not compromise patient safety given the benefit/ risk of secukinumab had already been assessed and secukinumab was registered in all participating countries. 2. Different aspects of the protocol were clarified following the review of different Ethics Committees (ECs): Clarification was made in the patient population that patients must have had an inadequate response to non-biologic DMARDs to be consistent with study rationale and primary objective of the study. The use of rescue medication was amended so it was less restrictive throughout the study and to make it more ethical for the patients randomized to placebo during the first 12 weeks given the risk of potential flare and existence of alternative therapies.

27 November 2018	The sample size calculation in the trial was updated keeping in mind the difficulties of recruitment. The initial sample size calculation for this trial was extrapolated from anbultrasound study assessed to evaluate the early response of abatacept on synovitis in patients with rheumatoid arthritis (D'Agostino et al 2016a) given the lack of a previous ultrasound PsA trial with biologics. A blinded sample size re-estimation was supplemented with data from the first 72 patients who reached their Week 12 visit to provide the most accurate estimation. The sample size was adjusted to a new target of 164 patients in total (82 patients per arm). This was the mid-way point of the range plus a 5% adjustment based on the dropout rate of patients prior to Week 12 observed at the time of this calculation. The reduction of sample size from 218 to 164 patients helped achieve completion of the last patient first visit by the end of August 2019. 2. Different aspects of the protocol were clarified following comments from the Health Authorities (HA), Ethics Committees and investigators. a. The dose of non-steroidal anti-inflammatory drugs (NSAIDs) as rescue therapy prior to assessments in the trial until Week 24 was clarified. The requirement for patients to return to their previous NSAIDs' dose following a transient increase in dose as rescue therapy 48 hours prior to study assessments was considered unethical by investigators and not accepted by patients who were in pain, and was therefore removed from the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported