Clinical trial results:
A randomized, double-blind, placebo-controlled multicenter study of subcutaneous secukinumab to demonstrate efficacy in the treatment of enthesitis at the Achilles tendon up to 1 year in adult patients with active Psoriatic Arthritis (PsA) and axial Spondyloarthritis (axSpA) (ACHILLES)

Summary

EudraCT number	2016-000972-91
Trial protocol	DE GB ES SK CZ GR BG IT
Global end of trial date	11 December 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	CAIN457F3301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02771210
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	CH-4200, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharmaceuticals, 41 613241111, 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	18 September 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate that the efficacy of secukinumab was superior to placebo based on the percentage of patients with resolution of Achilles tendon enthesitis as assessed by the respective subcomponent of the Leeds enthesitis index (LEI) at 24 weeks in patients with active PsA and axSpA.

Protection of trial subjects:

The 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	30 August 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 21
Country: Number of subjects enrolled	Czechia: 40
Country: Number of subjects enrolled	Germany: 54
Country: Number of subjects enrolled	Greece: 11
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Slovakia: 2
Country: Number of subjects enrolled	Spain: 36
Country: Number of subjects enrolled	United Kingdom: 25
Worldwide total number of subjects	204
EEA total number of subjects	204

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)	192
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

304 patients were screened. Of these, 94 patients discontinued during screening phase, 6 patients were re-screened and 204 patients completed the screening phase and were randomized in the trial.

Pre-assignment

Screening details:

A total of 175 patients (85.8%) completed treatment period 1 (up to Week 24); 29 patients (14.2%) discontinued study treatment in treatment period 1. A total of 170 patients (83.3%) completed treatment period 2 (up to Week 52); 5 patients (2.5%) discontinued in treatment period 2.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab

Arm description:

Secukinumab 150 mg or 300 mg s.c., administered at baseline, weeks 1, 2, 3, 4 and every 4 weeks until week 24, respective dose was assigned according to underlying condition, in case of PsA according to severity of concomitant Psoriasis or preexposure to anti-TNFα

Arm type	Experimental
Investigational medicinal product name	AIN457
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution and suspension for suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Secukinumab as one (1.0 mL PFS of 150 mg dose) or two (2 × 1.0 mL PFS of 150 mg dose, 300 mg) s.c. injections according to axSpA or PsA disease at Baseline, Week 1, Week 2, and Week 3, followed by administration every 4 weeks starting at Week 4.

Arm title	Placebo

Arm description:

Placebo 150 mg or 300 mg s.c., administered at baseline, weeks 1, 2, 3, 4 and every 4 weeks until week 24, respective dose was assigned according to underlying condition, in case of PsA according to severity of concomitant Psoriasis or preexposure to anti-TNFα

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

Dosage and administration details:

Placebo as one (1.0 mL PFS of 150 mg dose) or two (2 × 1.0 mL PFS of 150 mg dose, 300 mg) s.c. injections according to axSpA or PsA disease at Baseline, Week 1, Week 2, and Week 3, followed by administration every 4 weeks starting at Week 4.

Number of subjects in period 1	Secukinumab	Placebo
Started	102	102
Completed	91	84
Not completed	11	18
Physician decision	-	1
Consent withdrawn by subject	-	3
Adverse event, non-fatal	5	3
Lost to follow-up	2	-
Withdrawal of informed consent	1	5
Lack of efficacy	3	6

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Period 2 has no loading and all patients received Secukinumab - no Placebo in this period. Open-label

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab

Arm description:

From week 24 Secukinumab 150 mg or 300 mg s.c. was administered every 4 weeks; respective dose was assigned according to underlying condition, in case of PsA according to severity of concomitant Psoriasis or preexposure to anti-TNFα

Arm type	Experimental
Investigational medicinal product name	AIN457
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Secukinumab as one (1.0 mL PFS of 150 mg dose) or two (2 × 1.0 mL PFS of 150 mg dose, 300 mg) s.c. injections according to axSpA or PsA disease at Baseline, Week 1, Week 2, and Week 3, followed by administration every 4 weeks starting at Week 4.

Arm title	Placebo/Secukinumab

Arm description:

From week 24 Secukinumab 150 mg or 300 mg s.c. was administered every 4 weeks; respective dose was assigned according to underlying condition, in case of PsA according to severity of concomitant Psoriasis or preexposure to anti-TNFα

Arm type	Placebo

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe, Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

placebo as one (1.0 mL PFS of 150 mg dose) or two (2 × 1.0 mL PFS of 150 mg dose, 300 mg) s.c. injections according to axSpA or PsA disease at Baseline, Week 1, Week 2, and Week 3, followed by administration every 4 weeks starting at Week 4.

Number of subjects in period 2	Secukinumab	Placebo/Secukinumab
Started	91	84
Completed	89	81
Not completed	2	3
Consent withdrawn by subject	1	-
Adverse event, non-fatal	1	-
Withdrawal of informed consent	-	2
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab
Reporting group description:	
Secukinumab 150 mg or 300 mg s.c., administered at baseline, weeks 1, 2, 3, 4 and every 4 weeks until week 24, respective dose was assigned according to underlying condition, in case of PsA according to severity of concomitant Psoriasis or preexposure to anti-TNFα	
Reporting group title	Placebo
Reporting group description:	
Placebo 150 mg or 300 mg s.c., administered at baseline, weeks 1, 2, 3, 4 and every 4 weeks until week 24, respective dose was assigned according to underlying condition, in case of PsA according to severity of concomitant Psoriasis or preexposure to anti-TNFα	

Reporting group values	Secukinumab	Placebo	Total
Number of subjects	102	102	204
Age Categorical			
Number of participants in each age group			
Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	97	95	192
>=65 years	5	7	12
Age Continuous			
Mean age of participants in each group			
Units: Years			
arithmetic mean	47.8	47.7	
standard deviation	± 11.33	± 11.02	-
Sex/Gender, Customized			
Number of males vs females in Randomized set			
Units: Participants			
Female	58	55	113
Male	44	47	91
Race/Ethnicity, Customized			
Number of participants (Randomized set) by race			
Units: Subjects			
Caucasian	99	99	198
Black	0	0	0
Asian	2	1	3
Other	1	2	3

End points

End points reporting groups

Reporting group title	Secukinumab
Reporting group description:	
Secukinumab 150 mg or 300 mg s.c., administered at baseline, weeks 1, 2, 3, 4 and every 4 weeks until week 24, respective dose was assigned according to underlying condition, in case of PsA according to severity of concomitant Psoriasis or preexposure to anti-TNFα	
Reporting group title	Placebo
Reporting group description:	
Placebo 150 mg or 300 mg s.c., administered at baseline, weeks 1, 2, 3, 4 and every 4 weeks until week 24, respective dose was assigned according to underlying condition, in case of PsA according to severity of concomitant Psoriasis or preexposure to anti-TNFα	
Reporting group title	Secukinumab
Reporting group description:	
From week 24 Secukinumab 150 mg or 300 mg s.c. was administered every 4 weeks; respective dose was assigned according to underlying condition, in case of PsA according to severity of concomitant Psoriasis or preexposure to anti-TNFα	
Reporting group title	Placebo/Secukinumab
Reporting group description:	
From week 24 Secukinumab 150 mg or 300 mg s.c. was administered every 4 weeks; respective dose was assigned according to underlying condition, in case of PsA according to severity of concomitant Psoriasis or preexposure to anti-TNFα	

Primary: Number (%) of patients with resolution of Achilles tendon enthesitis

End point title	Number (%) of patients with resolution of Achilles tendon enthesitis
End point description:	
Number (%) of patients with resolution of Achilles tendon enthesitis (affected foot) as assessed by respective subcomponent of Leeds enthesitis index (LEI) at Week 24. The primary analysis was performed via a logistic regression model with the factors treatment, country, and stratification factor diagnosis (PsA or axSpA); patients with a missing assessment were considered as responders if they had already met the response criterion at the time of last assessment.	
End point type	Primary
End point timeframe:	
Week 24	

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	102		
Units: Participants	43	32		

Statistical analyses

Statistical analysis title	Resolution of achilles tendon enthesitis

Statistical analysis description:

The primary analysis was performed via a logistic regression model with the factors treatment, country, and stratification factor diagnosis (PsA or axSpA); patients with a missing assessment were considered as responders if they had already met the response criterion at the time of last assessment.

Comparison groups	Secukinumab v Placebo
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.136
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	3.08

Secondary: Mean change of heel pain

End point title	Mean change of heel pain

End point description:

Mean change of heel pain from baseline to Week 24 measured by Numeric Rating Scale (NRS) ranging from 0 to 10, with 0 representing no pain and 10 representing worst pain (e.g. "pain as bad as you can imagine" or "worst pain imaginable").

End point type	Secondary

End point timeframe:

Week 24

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	85		
Units: Mean				
arithmetic mean (standard deviation)	-2.8 (± 2.99)	-1.9 (± 2.69)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number (%) of patients with improvement of bone marrow edema

End point title	Number (%) of patients with improvement of bone marrow edema

End point description:

Number (%) of patients with an improvement of bone marrow edema from baseline to Week 24 as assessed by the respective subcomponent of the Psoriatic Arthritis Magnetic Resonance Imaging Score (PsAMRIS) in the affected foot.

End point type	Secondary

End point timeframe:

Week 24

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	36		
Units: Participants	17	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Number (%) of patients with resolution of enthesitis as assessed by LEI

End point title	Number (%) of patients with resolution of enthesitis as assessed by LEI

End point description:

Number (%) of patients with resolution of enthesitis as assessed by the Leeds enthesitis index (LEI) at Week 24.

End point type	Secondary

End point timeframe:

Week 24

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	102		
Units: Participants	31	21		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change of physician’s global assessment (PhGA) of disease activity

End point title	Mean change of physician’s global assessment (PhGA) of disease activity

End point description:

Mean change of physician’s global assessment (PhGA) of disease activity from baseline to Week 24 measured by Visual Analog Scale (VAS) ranging from 0 to 100, with 0 representing not severe and 100 representing very severe.

End point type	Secondary

End point timeframe:

Week 24

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	85		
Units: mm				
arithmetic mean (standard deviation)	-34.88 (± 25.927)	-18.93 (± 26.257)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change of patient’s global assessment (PGA) of disease activity

End point title	Mean change of patient’s global assessment (PGA) of disease activity

End point description:

Mean change of patient’s global assessment (PGA) of disease activity from baseline to Week 24 measured by Visual Analog Scale (VAS) ranging from 0 to 100, with 0 representing not severe and 100 representing very severe.

End point type	Secondary

End point timeframe:

Week 24

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	80		
Units: mm				
arithmetic mean (standard deviation)	-25.87 (± 31.108)	-16.61 (± 29.235)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change of physician’s assessment of heel enthesopathy activity

End point title	Mean change of physician’s assessment of heel enthesopathy activity

End point description:

Mean change of physician’s assessment of heel enthesopathy activity from baseline to Week 24 measured by Visual Analog Scale (VAS) ranging from 0 to 100, with 0 representing not severe and 100 representing very severe.

End point type	Secondary

End point timeframe:

Week 24

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	85		
Units: mm				
arithmetic mean (standard deviation)	-38.40 (± 24.244)	-25.19 (± 25.250)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change of patient’s assessment of heel enthesopathy activity

End point title	Mean change of patient’s assessment of heel enthesopathy activity

End point description:

Mean change of patient’s assessment of heel enthesopathy activity from baseline to Week 24 measured by Visual Analog Scale (VAS) ranging from 0 to 100, with 0 representing not severe and 100 representing very severe.

End point type	Secondary

End point timeframe:

Week 24

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	84		
Units: mm				
arithmetic mean (standard deviation)	-31.05 (± 29.135)	-20.77 (± 30.417)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in Short Form-36 (SF-36) v2

End point title	Mean change in Short Form-36 (SF-36) v2

End point description:

Mean change in Short Form-36 (SF-36) v2 as an indicator of overall health status

The SF-36 has eight scaled scores; the scores are weighted sums of the questions in each section. Lower scores = more disability, higher scores = less disability

End point type	Secondary

End point timeframe:

Week 24

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	85		
Units: scores on a scale				
arithmetic mean (standard deviation)	8.29 (± 9.759)	5.28 (± 7.285)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number (%) of patients with resolution of achilles tendon enthesitis after switching from placebo to secukinumab

End point title	Number (%) of patients with resolution of achilles tendon enthesitis after switching from placebo to secukinumab

End point description:

To describe the increase in percentage of patients with resolution of achilles tendon enthesitis (affected foot) after switching from placebo to secukinumab at Week 24.

End point type	Secondary

End point timeframe:

Weeks 24 and 52

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	102		
Units: Participants				
Week 24	43	32		
Week 52	66	55		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change of heel pain after switching from placebo to secukinumab

End point title	Mean change of heel pain after switching from placebo to secukinumab

End point description:

To describe the increase in mean change of heel pain after switching from placebo to secukinumab at Week 24.

End point type	Secondary

End point timeframe:

Weeks 24 and 52

End point values	Secukinumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	79		
Units: Mean				
arithmetic mean (standard deviation)	-0.70 (± 2.291)	-1.43 (± 2.251)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first dose of study treatment until end of study at week 52

Adverse event reporting additional description:

Adverse Events (AEs) are any untoward sign or symptom that occurs during the study treatment. Where a patient reported more than 1 AE with the same preferred term, the AE was counted only once; and where a patient reported more than 1 AE within the same primary system organ class, patient was counted only once at the system organ class level.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Secukinumab

Reporting group description:

Secukinumab

Reporting group title	Placebo/Placebo-Secukinumab

Reporting group description:

Placebo/Placebo-Secukinumab

Serious adverse events	Secukinumab	Placebo/Placebo-Secukinumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 102 (6.86%)	6 / 102 (5.88%)	
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)			
Invasive breast carcinoma			
subjects affected / exposed	1 / 102 (0.98%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 102 (0.98%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cancer			
subjects affected / exposed	0 / 102 (0.00%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Venous thrombosis limb			
subjects affected / exposed	0 / 102 (0.00%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 102 (0.98%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cauda equina syndrome			
subjects affected / exposed	1 / 102 (0.98%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine with aura			
subjects affected / exposed	1 / 102 (0.98%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 102 (0.00%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammatory bowel disease			

subjects affected / exposed	1 / 102 (0.98%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal stenosis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 102 (0.00%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 102 (0.98%)	0 / 102 (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			
Cellulitis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 102 (0.00%)	1 / 102 (0.98%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Secukinumab	Placebo/Placebo-Secukinumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 102 (32.35%)	34 / 102 (33.33%)	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 102 (5.88%)	10 / 102 (9.80%)	
occurrences (all)	8	16	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 102 (7.84%)	5 / 102 (4.90%)	
occurrences (all)	8	5	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 102 (6.86%)	5 / 102 (4.90%)	
occurrences (all)	8	8	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	13 / 102 (12.75%)	22 / 102 (21.57%)	
occurrences (all)	18	28	
Upper respiratory tract infection			
subjects affected / exposed	6 / 102 (5.88%)	5 / 102 (4.90%)	
occurrences (all)	6	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported