Clinical trial results:
A randomized, double-blind, active control, multicenter study to evaluate the efficacy at week 52 of subcutaneously administered secukinumab monotherapy compared with subcutaneously administered adalimumab monotherapy in patients with active psoriatic arthritis

Summary

EudraCT number	2015-004477-32
Trial protocol	DE FR AT GB ES GR SK DK FI NL CZ PT HU IS BG LT LV PL IT
Global end of trial date	30 December 2019

Results information

Result version number	v2 (current)
This version publication date	25 March 2021
First version publication date	24 December 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CAIN457F2366

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02745080
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	Clinical Disclosure Office, Novartis Pharma AG, 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	30 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 December 2019
Global end of trial reached?	Yes
Global end of trial date	30 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate that the efficacy of secukinumab monotherapy (300 mg s.c.) at Week 52 is superior to adalimumab monotherapy (40 mg s.c.), based on the proportion of patients achieving an American College of Rheumatology 20 (ACR20) response:

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	03 April 2017
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	Australia: 33
Country: Number of subjects enrolled	Bulgaria: 28
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Czechia: 80
Country: Number of subjects enrolled	Denmark: 17
Country: Number of subjects enrolled	Estonia: 28
Country: Number of subjects enrolled	Finland: 14
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Germany: 65
Country: Number of subjects enrolled	Greece: 24
Country: Number of subjects enrolled	Hungary: 22
Country: Number of subjects enrolled	Iceland: 5
Country: Number of subjects enrolled	India: 23
Country: Number of subjects enrolled	Israel: 31
Country: Number of subjects enrolled	Italy: 25
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	Latvia: 7
Country: Number of subjects enrolled	Lithuania: 34
Country: Number of subjects enrolled	Netherlands: 8

Country: Number of subjects enrolled	Poland: 35
Country: Number of subjects enrolled	Portugal: 13
Country: Number of subjects enrolled	Russian Federation: 99
Country: Number of subjects enrolled	Slovakia: 21
Country: Number of subjects enrolled	Spain: 94
Country: Number of subjects enrolled	United Kingdom: 74
Country: Number of subjects enrolled	United States: 43
Worldwide total number of subjects	853
EEA total number of subjects	534

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)	756
From 65 to 84 years	97
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 161 centers in 26 countries worldwide: Australia, Bulgaria, Canada, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, India, Israel, Italy, South Korea, Latvia, Lithuania, The Netherlands, Poland, Portugal, Russia, Slovakia, Spain, UK and USA.

Pre-assignment

Screening details:

853 patients were randomized in a 1:1 ratio to receive secukinumab 300 mg (N=426) or adalimumab 40 mg (N=427); All randomized patients were analyzed for efficacy and safety.

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	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab 300 mg s.c.

Arm description:

Secukinumab 300 mg administered at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 48.

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

Dosage and administration details:

Secukinumab 300 mg s.c injection (2 x 1 mL PFS) was administered at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks to Week 48.

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 (1 x 1 mL PFS) at given visits in order to maintain the blind

Arm title	Adalimumab 40 mg s.c.

Arm description:

Adalimumab 40 mg administered at Baseline followed by dosing every 2 weeks until Week 50.

Arm type	Active comparator
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 (1 x 0.5 mL or 2 x 0.5 mL PFS) at given visits in order to maintain the blind

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

Dosage and administration details:

Adalimumab (40 mg) s.c. injection was available in 1 x 0.4 mL PFS and administered at Baseline followed by dosing every 2 weeks until Week 50

Number of subjects in period 1	Secukinumab 300 mg s.c.	Adalimumab 40 mg s.c.
Started	426	427
Completed	371	338
Not completed	55	89
Physician decision	3	-
Consent withdrawn by subject	22	41
Adverse event, non-fatal	13	21
Lost to follow-up	3	3
Lack of efficacy	11	23
Protocol deviation	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab 300 mg s.c.
Reporting group description:	
Secukinumab 300 mg administered at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 48.	
Reporting group title	Adalimumab 40 mg s.c.
Reporting group description:	
Adalimumab 40 mg administered at Baseline followed by dosing every 2 weeks until Week 50.	

Reporting group values	Secukinumab 300 mg s.c.	Adalimumab 40 mg s.c.	Total
Number of subjects	426	427	853
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	386	370	756
From 65-84 years	40	57	97
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	48.5	49.5	
standard deviation	± 12.38	± 12.44	-
Sex: Female, Male Units: Participants			
Female	218	198	416
Male	208	229	437
Race/Ethnicity, Customized Units: Subjects			
Asian	16	20	36
American Indian or Alaska Native	0	1	1
Black or African American	3	2	5
White	402	391	793
Unknown	1	5	6
Other	4	8	12

End points

End points reporting groups

Reporting group title	Secukinumab 300 mg s.c.
Reporting group description:	
Secukinumab 300 mg administered at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 48.	
Reporting group title	Adalimumab 40 mg s.c.
Reporting group description:	
Adalimumab 40 mg administered at Baseline followed by dosing every 2 weeks until Week 50.	

Primary: Percentage of Participants Who Achieved an American College of Rheumatology 20% (ACR20) Response at Week 52

End point title	Percentage of Participants Who Achieved an American College of Rheumatology 20% (ACR20) Response at Week 52
End point description:	
Clinical response, failure to permanently discontinue study medication prematurely, and lack of need for rescue medication was required for a patient to achieve treatment success. The primary endpoint is the proportion of patients with monotherapy ACR20 response at Week 52 where monotherapy ACR20 response is defined as meeting the following 3 conditions: 1. achieving American College of Rheumatology 20 (ACR20) response 2. no permanent study treatment (secukinumab or adalimumab) discontinuation before or at Week 50 (the last dosing visit) 3. no use of conventional disease modifying anti-rheumatic drugs (also known as non-biologic DMARDs) cDMARDs (including Methotrexate (MTX)) after Week 36 (regardless of the starting time of taking cDMARDs)	
End point type	Primary
End point timeframe:	
Week 52	

End point values	Secukinumab 300 mg s.c.	Adalimumab 40 mg s.c.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	426	427		
Units: Percentage of Participants				
number (confidence interval 95%)	67.4 (62.8 to 71.7)	61.5 (56.8 to 66.0)		

Statistical analyses

Statistical analysis title	ACR20 Response
Comparison groups	Secukinumab 300 mg s.c. v Adalimumab 40 mg s.c.

Number of subjects included in analysis	853
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0719
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.72

Secondary: Percentage of Participants Who Achieved a Psoriasis Area and Severity Index (PASI)-90 Response at Week 52

End point title	Percentage of Participants Who Achieved a Psoriasis Area and Severity Index (PASI)-90 Response at Week 52

End point description:

The PASI is a system used for assessing and grading the severity of psoriatic lesions. In the PASI system, the body is divided into 4 regions: the head, trunk, upper extremities, and lower extremities. Each of these areas were assessed separately for the percentage of the area involved, which translates to a numeric score that ranges from 0 to 6, and for erythema, induration, and scaling, which are each rated on a scale of 0 to 4. The PASI produces a numeric score that can range from 0 to 72. A higher score indicates more severe disease. A PASI 90 response represents participants who achieved at least a 90 percent improvement from baseline in the PASI score.

End point type	Secondary

End point timeframe:

Week 52

End point values	Secukinumab 300 mg s.c.	Adalimumab 40 mg s.c.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	215	202		
Units: Percentage of Participants				
number (confidence interval 95%)	65.4 (58.8 to 71.5)	43.2 (36.5 to 50.2)		

Statistical analyses

Statistical analysis title	PASI90 Response
Comparison groups	Secukinumab 300 mg s.c. v Adalimumab 40 mg s.c.

Number of subjects included in analysis	417
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.67
upper limit	3.71

Secondary: Percentage of Participants Who Achieved an American College of Rheumatology 50% (ACR50) Response at Week 52

End point title	Percentage of Participants Who Achieved an American College of Rheumatology 50% (ACR50) Response at Week 52

End point description:

Clinical response, failure to permanently discontinue study medication prematurely, and lack of need for rescue medication was required for a patient to achieve treatment success. The secondary endpoint is the proportion of patients with monotherapy ACR50 response at Week 52 where monotherapy ACR50 response is defined as meeting the following 3 conditions:
1. achieving American College of Rheumatology 50 (ACR50) response
2. no permanent study treatment (secukinumab or adalimumab) discontinuation before or at Week 52
3. no use of conventional disease modifying anti-rheumatic drugs (also known as non-biologic DMARDs) cDMARDs (including Methotrexate (MTX)) after Week 36 (regardless of the starting time of taking cDMARDs)

End point type	Secondary

End point timeframe:

Week 52

End point values	Secukinumab 300 mg s.c.	Adalimumab 40 mg s.c.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	426	427		
Units: Percentage of Participants				
number (confidence interval 95%)	49.0 (44.3 to 53.7)	44.8 (40.1 to 49.5)		

Statistical analyses

Statistical analysis title	ACR50 Response
Comparison groups	Secukinumab 300 mg s.c. v Adalimumab 40 mg s.c.

Number of subjects included in analysis	853
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2251
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.55

Secondary: Change from Baseline in Health Assessment Questionnaire – Disability Index (HAQ-DI score) at Week 52

End point title	Change from Baseline in Health Assessment Questionnaire – Disability Index (HAQ-DI score) at Week 52

End point description:

The HAQ-DI assesses a subject's level of functional ability and includes questions of fine movements of the upper extremity, locomotor activities of the lower extremity, and activities that involve both upper and lower extremities. There are 20 questions in 8 categories of functioning including dressing, rising, eating, walking, hygiene, reach, grip and usual activities. The stem of each item asks 'Over the past week, "are you able to..." perform a particular task'. Each item is scored on a 4 point scale from 0 - 3, representing normal, no difficulty (0), some difficulty (1), much difficulty (2) and unable to do (3). The disability index score is calculated as the mean of the available category scores, ranging from 0 to 3. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Secukinumab 300 mg s.c.	Adalimumab 40 mg s.c.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	426	427		
Units: Unit on a scale				
least squares mean (standard error)	-0.58 (± 0.027)	-0.56 (± 0.027)		

Statistical analyses

Statistical analysis title	HAQ-DI Score
Comparison groups	Secukinumab 300 mg s.c. v Adalimumab 40 mg s.c.

Number of subjects included in analysis	853
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5465
Method	Mixed models analysis
Parameter estimate	least squares (LS) mean change
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.038

Secondary: Percentage of Participants Who Achieved Resolution of enthesitis at Week 52

End point title	Percentage of Participants Who Achieved Resolution of enthesitis at Week 52

End point description:

Enthesitis refers to inflammation of entheses, the site where ligaments or tendons insert into the bones. Resolution was defined as the absence of recorded enthesitis; conducted by the study assessor.

End point type	Secondary

End point timeframe:

Week 52

End point values	Secukinumab 300 mg s.c.	Adalimumab 40 mg s.c.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	264		
Units: Percentage of Participants				
number (confidence interval 95%)	60.5 (54.1 to 66.6)	54.2 (48.2 to 60.2)		

Statistical analyses

Statistical analysis title	Resolution of Enthesitis
Comparison groups	Secukinumab 300 mg s.c. v Adalimumab 40 mg s.c.
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1498
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.87

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events were collected from first dose of study treatment until 12 Weeks (84 days) following the last administration of study treatment, an average of 68 weeks.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	AIN457 300 mg

Reporting group description:

AIN457 300 mg

Reporting group title	Adalimumab 40 mg

Reporting group description:

Adalimumab 40 mg

Reporting group title	Total

Reporting group description:

Total

Serious adverse events	AIN457 300 mg	Adalimumab 40 mg	Total
Total subjects affected by serious adverse events			
subjects affected / exposed	37 / 426 (8.69%)	36 / 427 (8.43%)	73 / 853 (8.56%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Leiomyoma			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Hodgkin's lymphoma			

subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasma cell myeloma			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial sarcoma			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Reproductive system and breast disorders			
Endometrial hypertrophy			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	1 / 426 (0.23%)	1 / 427 (0.23%)	2 / 853 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	0 / 426 (0.00%)	2 / 427 (0.47%)	2 / 853 (0.23%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Alveolitis			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			

subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 426 (0.23%)	1 / 427 (0.23%)	2 / 853 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epicondylitis			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Foot fracture			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post-traumatic neck syndrome			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIIIth nerve injury			

subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 426 (0.47%)	0 / 427 (0.00%)	2 / 853 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Horner's syndrome			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial aneurysm			

subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculopathy			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	2 / 426 (0.47%)	0 / 427 (0.00%)	2 / 853 (0.23%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall haematoma			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic artery aneurysm			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholecystitis			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perioral dermatitis			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical spinal stenosis			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			

subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 426 (0.23%)	1 / 427 (0.23%)	2 / 853 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriatic arthropathy			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis infective			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			

subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis salmonella			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abscess			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Labyrinthitis			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection fungal			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Measles			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mycobacterial infection			
subjects affected / exposed	0 / 426 (0.00%)	1 / 427 (0.23%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal cyst			

subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 426 (0.00%)	3 / 427 (0.70%)	3 / 853 (0.35%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Puncture site abscess			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	1 / 426 (0.23%)	0 / 427 (0.00%)	1 / 853 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	AIN457 300 mg	Adalimumab 40 mg	Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	226 / 426 (53.05%)	236 / 427 (55.27%)	462 / 853 (54.16%)
Vascular disorders			
Hypertension			
subjects affected / exposed	27 / 426 (6.34%)	24 / 427 (5.62%)	51 / 853 (5.98%)
occurrences (all)	28	23	51
Nervous system disorders			
Headache			
subjects affected / exposed	36 / 426 (8.45%)	33 / 427 (7.73%)	69 / 853 (8.09%)
occurrences (all)	49	43	92
General disorders and administration site conditions			

Injection site reaction			
subjects affected / exposed	4 / 426 (0.94%)	28 / 427 (6.56%)	32 / 853 (3.75%)
occurrences (all)	5	118	123
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	32 / 426 (7.51%)	37 / 427 (8.67%)	69 / 853 (8.09%)
occurrences (all)	40	41	81
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	24 / 426 (5.63%)	14 / 427 (3.28%)	38 / 853 (4.45%)
occurrences (all)	27	16	43
Oropharyngeal pain			
subjects affected / exposed	25 / 426 (5.87%)	15 / 427 (3.51%)	40 / 853 (4.69%)
occurrences (all)	34	16	50
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	33 / 426 (7.75%)	34 / 427 (7.96%)	67 / 853 (7.85%)
occurrences (all)	38	45	83
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	29 / 426 (6.81%)	31 / 427 (7.26%)	60 / 853 (7.03%)
occurrences (all)	33	43	76
Back pain			
subjects affected / exposed	17 / 426 (3.99%)	31 / 427 (7.26%)	48 / 853 (5.63%)
occurrences (all)	21	31	52
Psoriatic arthropathy			
subjects affected / exposed	34 / 426 (7.98%)	38 / 427 (8.90%)	72 / 853 (8.44%)
occurrences (all)	25	35	60
Infections and infestations			
Bronchitis			
subjects affected / exposed	16 / 426 (3.76%)	27 / 427 (6.32%)	43 / 853 (5.04%)
occurrences (all)	17	28	45
Nasopharyngitis			
subjects affected / exposed	88 / 426 (20.66%)	84 / 427 (19.67%)	172 / 853 (20.16%)
occurrences (all)	115	117	232
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	42 / 426 (9.86%) 59	54 / 427 (12.65%) 65	96 / 853 (11.25%) 124

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 January 2017	At the time of this amendment, no patients had been randomized into the study. No change to the study population was proposed by this amendment. This protocol amendment was primarily issued for the following reasons: 1) The half-life of adalimumab is reported to be approximately 2 weeks, therefore in the original protocol the safety follow-up was planned to cover 5x the half-life or approximately 10 weeks. Consequently, the safety follow-up visit was scheduled for 10 weeks after the last dose of adalimumab. 2) Exclusion Criteria 2 provided guidelines and examples where local label requirements for contraception use, after the last dose of study treatment, should be followed by women of childbearing potential. Health Authority requests stipulated that the protocol should specify contraception use for 5 months after last dose of adalimumab (see Humira® SmPC 2019).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32386593