Clinical trial results:
Secukinumab In patients with moderate to severe active, chronic plaque psoriasis who have failed on tumor necrosis factor alpha (TNF) antaGoNists: A clinical Trial EvalUating Treatment REsults

Summary

EudraCT number	2013-001855-11
Trial protocol	GB IE
Global end of trial date	12 July 2016

Results information

Result version number	v1 (current)
This version publication date	02 February 2018
First version publication date	02 February 2018

Trial information

Trial identification

Sponsor protocol code	CAIN457AGB01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01961609
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 4163241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 4163241111,

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	12 July 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the efficacy of secukinumab (300mg) treatment with respect to PASI 75 response rate after 16 weeks treatment, by assessing the percentage (%) of patients achieving PASI 75 after 16 weeks compared to baseline (defined as PASI status at Week 0).

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	09 October 2013
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	Ireland: 12
Country: Number of subjects enrolled	United Kingdom: 223
Worldwide total number of subjects	235
EEA total number of subjects	235

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)	223
From 65 to 84 years	12

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study consisted of 3 periods: initiation, maintenance 1 and maintenance 2. During the initiation period, participants received secukinumab 150 mg or 300 mg for 16 weeks.

Pre-assignment

Screening details:

For both maintenance periods 1 and 2, after 16 weeks and 48 weeks, respectively, responders at both the 150 mg and 300 mg doses continued on their initiation doses during maintenance periods 1 and 2. Non-responders at 150 mg were uptitrated to 300 mg. Non-responders at 300 mg returned to routine treatment under the care of their usual clinician.

Period 1

Period 1 title	Initiation (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab (AIN457) 300 mg

Arm description:

Participants self-administered 300 mg secukinumab loading dose subcutaneously at Day 0 (initiation of study drug) and at weeks 1, 2, 3 & 4, and then every 4 weeks. Following the Primary Endpoint at 16 weeks, participants meeting the National Institute for Health and Care Excellence (NICE) criteria of adequate response were eligible to continue on study treatment for a further 32 weeks. Participants not meeting this NICE criterion returned to routine treatment under the care of their usual Clinical Team. Following assessment at week 48, participants meeting the NICE criteria of adequate response were eligible to continue on study treatment for a further 24 weeks. Participants not meeting this NICE criterion returned to routine treatment under the care of their usual Clinical Team.

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

Dosage and administration details:

Participants self-administered 300 mg secukinumab loading dose subcutaneously at Day 0 (initiation of study drug) and at weeks 1, 2, 3 & 4, and then every 4 weeks. Following the Primary Endpoint at 16 weeks, participants meeting the National Institute for Health and Care Excellence (NICE) criteria of adequate response were eligible to continue on study treatment for a further 32 weeks. Participants not meeting this NICE criterion returned to routine treatment under the care of their usual Clinical Team. Following assessment at week 48, participants meeting the NICE criteria of adequate response were eligible to continue on study treatment for a further 24 weeks. Participants not meeting this NICE criterion returned to routine treatment under the care of their usual Clinical Team.

Arm title	Secukinumab (AIN457) 150 mg

Arm description:

Participants self-administered secukinumab 150 mg loading dose subcutaneously at Day 0 (initiation of study drug), weeks 1, 2, 3 & 4 and then every 4 weeks. Following the Primary Endpoint at 16 weeks, participants meeting the NICE criteria of adequate response were eligible to continue on study treatment for a further 32 weeks at the 150mg dose. Participants not achieving the NICE criteria at the Primary Endpoint were up titrated to 300mg at the discretion of the treating physician. Following assessment at week 48, participants meeting the NICE criteria of adequate response were eligible to continue on study treatment for a further 24 weeks at the 150mg dose. Participants not achieving the NICE criteria at 48 weeks on the 150mg dose were up titrated to 300mg at the discretion of the treating physician.

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

Dosage and administration details:

Participants self-administered secukinumab 150 mg loading dose subcutaneously at Day 0 (initiation of study drug), weeks 1, 2, 3 & 4 and then every 4 weeks. Following the Primary Endpoint at 16 weeks, participants meeting the NICE criteria of adequate response were eligible to continue on study treatment for a further 32 weeks at the 150mg dose. Participants not achieving the NICE criteria at the Primary Endpoint were up titrated to 300mg at the discretion of the treating physician. Following assessment at week 48, participants meeting the NICE criteria of adequate response were eligible to continue on study treatment for a further 24 weeks at the 150mg dose. Participants not achieving the NICE criteria at 48 weeks on the 150mg dose were up titrated to 300mg at the discretion of the treating physician.

Number of subjects in period 1	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg
Started	119	116
Safety set	118	115
Full analysis set	118	115
Completed	107	103
Not completed	12	13
Adverse event, serious fatal	-	1
Consent withdrawn by subject	1	2
Adverse event, non-fatal	3	5
Randomized but not treated	1	1
Protocol deviation	1	-
Administrative problems	1	-
Abnormal lab values	-	1
Missing	3	2
Lack of efficacy	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab (AIN457) 300 mg

Reporting group description:

Participants self-administered 300 mg secukinumab loading dose subcutaneously at Day 0 (initiation of study drug) and at weeks 1, 2, 3 & 4, and then every 4 weeks. Following the Primary Endpoint at 16 weeks, participants meeting the National Institute for Health and Care Excellence (NICE) criteria of adequate response were eligible to continue on study treatment for a further 32 weeks. Participants not meeting this NICE criterion returned to routine treatment under the care of their usual Clinical Team. Following assessment at week 48, participants meeting the NICE criteria of adequate response were eligible to continue on study treatment for a further 24 weeks. Participants not meeting this NICE criterion returned to routine treatment under the care of their usual Clinical Team.

Reporting group title	Secukinumab (AIN457) 150 mg

Reporting group description:

Participants self-administered secukinumab 150 mg loading dose subcutaneously at Day 0 (initiation of study drug), weeks 1, 2, 3 & 4 and then every 4 weeks. Following the Primary Endpoint at 16 weeks, participants meeting the NICE criteria of adequate response were eligible to continue on study treatment for a further 32 weeks at the 150mg dose. Participants not achieving the NICE criteria at the Primary Endpoint were up titrated to 300mg at the discretion of the treating physician. Following assessment at week 48, participants meeting the NICE criteria of adequate response were eligible to continue on study treatment for a further 24 weeks at the 150mg dose. Participants not achieving the NICE criteria at 48 weeks on the 150mg dose were up titrated to 300mg at the discretion of the treating physician.

Reporting group values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg	Total
Number of subjects	119	116	235
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)	114	109	223
From 65-84 years	5	7	12
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	46.6	44.6	
standard deviation	± 11.63	± 11.73	-
Gender, Male/Female			
Units: Subjects			
Female	51	52	103
Male	68	64	132

End points

End points reporting groups

Reporting group title	Secukinumab (AIN457) 300 mg

Reporting group description:

Participants self-administered 300 mg secukinumab loading dose subcutaneously at Day 0 (initiation of study drug) and at weeks 1, 2, 3 & 4, and then every 4 weeks. Following the Primary Endpoint at 16 weeks, participants meeting the National Institute for Health and Care Excellence (NICE) criteria of adequate response were eligible to continue on study treatment for a further 32 weeks. Participants not meeting this NICE criterion returned to routine treatment under the care of their usual Clinical Team. Following assessment at week 48, participants meeting the NICE criteria of adequate response were eligible to continue on study treatment for a further 24 weeks. Participants not meeting this NICE criterion returned to routine treatment under the care of their usual Clinical Team.

Reporting group title	Secukinumab (AIN457) 150 mg

Reporting group description:

Participants self-administered secukinumab 150 mg loading dose subcutaneously at Day 0 (initiation of study drug), weeks 1, 2, 3 & 4 and then every 4 weeks. Following the Primary Endpoint at 16 weeks, participants meeting the NICE criteria of adequate response were eligible to continue on study treatment for a further 32 weeks at the 150mg dose. Participants not achieving the NICE criteria at the Primary Endpoint were up titrated to 300mg at the discretion of the treating physician. Following assessment at week 48, participants meeting the NICE criteria of adequate response were eligible to continue on study treatment for a further 24 weeks at the 150mg dose. Participants not achieving the NICE criteria at 48 weeks on the 150mg dose were up titrated to 300mg at the discretion of the treating physician.

Subject analysis set title	Secukinumab (AIN457) 300 mg subgroup 1
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who had experienced an IR after trying the first anti-tumor necrosis factor-alpha (TNFalpha) therapy

Subject analysis set title	Secukinumab (AIN457) 300 mg subgroup 2
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who had initially experienced an adequate response after trying the first TNFalpha therapy, but then subsequently lost that response

Subject analysis set title	Secukinumab (AIN457) 300 mg subgroup 3
Subject analysis set type	Full analysis

Subject analysis set description:

All participants who have tried and failed more than one anti-TNFalpha therapies

Subject analysis set title	Secukinumab (AIN457) 150 mg subgroup 1
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who had experienced an IR after trying the first anti-tumor necrosis factor-alpha (TNFalpha) therapy

Subject analysis set title	Secukinumab (AIN457) 150 mg subgroup 2
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who had initially experienced an adequate response after trying the first TNFalpha therapy, but then subsequently lost that response

Subject analysis set title	Secukinumab (AIN457) 150 mg subgroup 3
Subject analysis set type	Full analysis

Subject analysis set description:

All participants who have tried and failed more than one anti-TNFalpha therapies

Subject analysis set title	Secukinumab (AIN457A) 300 mg subgroups 1 and 2 combined
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who experienced an IR after trying first anti-TNFalpha therapy and participants who had initially experienced an adequate response after trying the first anti-TNFalpha therapy but then had

subsequently lost that response.

Subject analysis set title	Secukinumab (AIN457) 150 mg subgroups 1 and 2 combined
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who experienced an IR after trying first anti-TNFalpha therapy and participants who had initially experienced an adequate response after trying the first anti-TNFalpha therapy but then had subsequently lost that response.

Subject analysis set title	Secukinumab (AIN457) 150 mg - 300 mg (Maintanence period 1)
Subject analysis set type	Full analysis

Subject analysis set description:

Non-responders at secukinumab 150mg from the initiation period were uptitrated to secukinumab 300 mg at week 16.

Subject analysis set title	Secukinumab (AIN457) 150 mg - 300 mg (Maintenance period 2)
Subject analysis set type	Full analysis

Subject analysis set description:

Non-responders at secukinumab 150 mg from maintenance 1 period were uptitrated to secukinumab 300 mg at week 48.

Primary: Percentage of secukinumab 300 mg participants achieving PASI 75 at 16 weeks

End point title	Percentage of secukinumab 300 mg participants achieving PASI 75 at 16 weeks[1][2]

End point description:

PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs); each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 75 is defined as participants achieving ≥ 75% improvement from baseline.

End point type	Primary

End point timeframe:

16 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis applies to the Secukinumab (AIN457) 300 mg group only.
Non-inferiority/equivalence test = No
P-Value: <0.0001
Method of estimation: 2-sided binomial exact test
Estimated value: 65.3 percent (A Bonferroni adjustment adjusting for 8 analyses have been applied.)
99.375% Confidence interval, 2-sided: 52.4 to 76.7

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: All arms do not apply to this end point.

End point values	Secukinumab (AIN457) 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: Percentage of participants				
number (not applicable)	65.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of secukinumab 150 mg participants achieving PASI 75 at 16 weeks

End point title	Percentage of secukinumab 150 mg participants achieving PASI 75 at 16 weeks[3]

End point description:

PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs); each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 75 is defined as participants achieving ≥ 75% improvement from baseline.

End point type	Secondary

End point timeframe:

16 Weeks

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: All arms do not apply to this end point.

End point values	Secukinumab (AIN457) 150 mg			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: Percentage of participants				
number (not applicable)	44.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving PASI 75 according to 3 key participant subgroups (Primary Inadequate Response (IR), Secondary IR and IR after more than one anti-TNFalpha therapies) at 16 weeks

End point title	Percentage of participants achieving PASI 75 according to 3 key participant subgroups (Primary Inadequate Response (IR), Secondary IR and IR after more than one anti-TNFalpha therapies) at 16 weeks

End point description:

PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs); each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and

desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 75 is defined as participants achieving ≥ 75% improvement from baseline.

End point type	Secondary

End point timeframe:

16 Weeks

End point values	Secukinumab (AIN457) 300 mg subgroup 1	Secukinumab (AIN457) 300 mg subgroup 2	Secukinumab (AIN457) 300 mg subgroup 3	Secukinumab (AIN457) 150 mg subgroup 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	44	44	18
Units: Percentage of participants				
number (not applicable)	71.4	70.5	47.7	38.9

End point values	Secukinumab (AIN457) 150 mg subgroup 2	Secukinumab (AIN457) 150 mg subgroup 3		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	42	37		
Units: Percentage of participants				
number (not applicable)	61.9	32.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieiving PASI 75 - Initiation Period

End point title	Percentage of participants achieiving PASI 75 - Initiation Period

End point description:

PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs); each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 75 is defined as participants achieving ≥ 75% improvement from baseline.

End point type	Secondary

End point timeframe:

2 ,4, 8, 12 and 16 Weeks

End point values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	115		
Units: Percentage of participants				
number (not applicable)				
Week 2	1.7	2.6		
Week 4	27.1	18.3		
Week 8	60.2	40.0		
Week 12	61.9	52.2		
Week 16	65.3	44.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieiving PASI 75 - Maintenance 1 Period

End point title	Percentage of participants achieiving PASI 75 - Maintenance 1 Period

End point description:

PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs); each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 75 is defined as participants achieving ≥ 75% improvement from baseline.

End point type	Secondary

End point timeframe:

16, 24 and 48 Weeks

End point values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg	Secukinumab (AIN457) 150 mg - 300 mg (Maintanence period 1)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	107	66	37	
Units: Percentage of participants				
number (not applicable)				
Week 16	72.0	75.8	2.7	
Week 24	61.7	68.2	13.5	
Week 48	52.3	39.4	8.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieiving PASI 75 - Maintenance 2 Period

End point title	Percentage of participants achieiving PASI 75 - Maintenance 2 Period

End point description:

PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs); each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 75 is defined as participants achieving ≥ 75% improvement from baseline.

End point type	Secondary

End point timeframe:

48 and 72 Weeks

End point values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg	Secukinumab (AIN457) 150 mg - 300 mg (Maintanence period 1)	Secukinumab (AIN457) 150 mg - 300 mg (Maintenance period 2)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	83	31	16	24
Units: Percentage of participants				
number (not applicable)				
Week 48	65.1	80.6	18.8	4.2
Week 72	65.1	58.1	25.0	37.5

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving PASI 50 and PASI 90 - Initiation Period

End point title	Percentage of participants achieving PASI 50 and PASI 90 - Initiation Period

End point description:

PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs); each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 50 and PASI 90 are defined as participants achieving ≥ 50% and ≥ 90% improvement from baseline, respectively.

End point type	Secondary

End point timeframe:

2, 4, 8, 12, 16 Weeks

End point values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	115		
Units: Percentage of participants				
number (not applicable)				
PASI 50, week 2	28.0	25.2		
PASI 50, week 4	63.6	57.4		
PASI 50, week 8	84.7	67.8		
PASI 50, week 12	82.2	69.6		
PASI 50, week 16	82.2	65.2		
PASI 90, week 2	0	0		
PASI 90, week 4	6.8	4.3		
PASI 90, week 8	25.4	20.0		
PASI 90, week 12	38.1	25.2		
PASI 90, week 16	41.5	20.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving PASI 50 and PASI 90 - Maintenance 1 Period

End point title	Percentage of participants achieving PASI 50 and PASI 90 - Maintenance 1 Period

End point description:

PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs); each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 50 and PASI 90 are defined as participants achieving ≥ 50% and ≥ 90% improvement from baseline, respectively.

End point type	Secondary

End point timeframe:

16, 24 and 48 Weeks

End point values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg	Secukinumab (AIN457) 150 mg - 300 mg (Maintanence period 1)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	107	66	37	
Units: Percentage of participants				

number (not applicable)				
PASI 50, week 16	89.7	95.5	24.3	
PASI 50, week 24	80.4	89.4	54.1	
PASI 50, week 48	70.1	65.2	32.4	
PASI 90, week 16	45.8	34.8	0	
PASI 90, week 24	39.3	37.9	2.7	
PASI 90, week 48	31.8	18.2	5.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving PASI 50 and PASI 90 - Maintenance 2 Period

End point title	Percentage of participants achieving PASI 50 and PASI 90 - Maintenance 2 Period

End point description:

PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs); each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 50 and PASI 90 are defined as participants achieving ≥ 50% and ≥ 90% improvement from baseline, respectively.

End point type	Secondary

End point timeframe:

48 and 72 Weeks

End point values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg	Secukinumab (AIN457) 150 mg - 300 mg (Maintanence period 1)	Secukinumab (AIN457) 150 mg - 300 mg (Maintenance period 2)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	83	31	16	24
Units: Percentage of participants				
number (not applicable)				
PASI 50, week 48	88.0	96.8	75.0	50.0
PASI 50, week 72	74.7	80.6	37.5	70.8
PASI 90, week 48	41.0	38.7	12.5	0
PASI 90, week 72	38.6	22.6	18.8	16.7

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who have failed on one anti-TNFα achieving

PASI 75 (subgroups 1 and 2 combined) at 16 weeks

End point title	Percentage of participants who have failed on one anti-TNFα achieving PASI 75 (subgroups 1 and 2 combined) at 16 weeks

End point description:

PASI is a combined assessment of lesion severity and affected area into a single score: 0 (no disease) to 72 (maximal disease). Body is divided into 4 areas for scoring (head, arms, trunk, legs); each area is scored by itself and scores are combined for final PASI. For each area, percent of skin involved is estimated: 0 (0%) to 6 (90-100%), and severity is estimated by clinical signs, erythema, induration and desquamation; scale 0 (none) to 4 (maximum). Final PASI = sum of severity parameters for each area* area score weight of section (head: 0.1, arms: 0.2 body: 0.3 legs: 0.4). PASI 75 is defined as participants achieving ≥ 75% improvement from baseline.

End point type	Secondary

End point timeframe:

16 Weeks

End point values	Secukinumab (AIN457A) 300 mg subgroups 1 and 2 combined	Secukinumab (AIN457) 150 mg subgroups 1 and 2 combined		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	58	60		
Units: Percentage of participants				
number (not applicable)	70.7	55.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving NICE continuation criteria (PASI 75 or PASI 50 plus a 5 point improvement in DLQI) at 16 weeks

End point title	Percentage of participants achieving NICE continuation criteria (PASI 75 or PASI 50 plus a 5 point improvement in DLQI) at 16 weeks

End point description:

PASI 75 is defined as participants achieving ≥ 75% improvement from baseline. The DLQI is a ten item general dermatology disability index designed to assess health-related quality of life in adult participants with skin diseases. The measure is widely used: it has been tested across 32 different skin conditions and is available in 55 languages. The DLQI total score is a sum of all 10 responses. Scores range from 0 to 30 with higher scores indicating greater health-related quality of life impairment.

End point type	Secondary

End point timeframe:

16 Weeks

End point values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	115		
Units: Percentage of participants				
number (not applicable)	81.4	60.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in Dermatology Life Quality Index (DLQI)Total scores - Initiation Period

End point title	Mean change from baseline in Dermatology Life Quality Index (DLQI)Total scores - Initiation Period

End point description:

The DLQI is a ten item general dermatology disability index designed to assess health-related quality of life in adult participants with skin diseases. The measure is widely used: it has been tested across 32 different skin conditions and is available in 55 languages. It is a self-administered questionnaire which includes domains of daily activity, leisure, personal relationships, symptoms and feelings, treatment and school/work activities. Each domain has 4 response categories ranging from 0 (not at all) to 3 (very much). "Not relevant" is a valid score also and is scored as 0. The DLQI total score is a sum of all 10 responses. Scores range from 0 to 30 with higher scores indicating greater health-related quality of life impairment. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

12 and 16 weeks

End point values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	115		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12, initiation (n=111,108)	-15.6 (± 7.49)	-13.2 (± 7.36)		
Week 16, initiation (n=109,103)	-16.1 (± 6.80)	-12.3 (± 7.68)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in Dermatology Life Quality Index (DLQI)Total scores - Maintenance 1 Period

End point title	Mean change from baseline in Dermatology Life Quality Index (DLQI)Total scores - Maintenance 1 Period

End point description:

The DLQI is a ten item general dermatology disability index designed to assess health-related quality of life in adult participants with skin diseases. The measure is widely used: it has been tested across 32 different skin conditions and is available in 55 languages. It is a self-administered questionnaire which includes domains of daily activity, leisure, personal relationships, symptoms and feelings, treatment and school/work activities. Each domain has 4 response categories ranging from 0 (not at all) to 3 (very much). "Not relevant" is a valid score also and is scored as 0. The DLQI total score is a sum of all 10 responses. Scores range from 0 to 30 with higher scores indicating greater health-related quality of life impairment. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

16, 24 and 48 weeks

End point values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg	Secukinumab (AIN457) 150 mg - 300 mg (Maintanence period 1)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	107	66	37	
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 16, maintenance 1 (n=106,64,36)	-16.3 (± 6.67)	-15.9 (± 6.31)	-6.1 (± 5.86)	
Week 24, maintenance 1(n=102,64,35)	-15.7 (± 7.25)	-14.4 (± 6.73)	-8.7 (± 6.01)	
Week 48, maintenance 1 (n=86, 55, 19)	-16.2 (± 8.06)	-11.5 (± 8.14)	-9.8 (± 6.76)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in Dermatology Life Quality Index (DLQI)Total scores - Maintenance 2 Period

End point title	Mean change from baseline in Dermatology Life Quality Index (DLQI)Total scores - Maintenance 2 Period

End point description:

The DLQI is a ten item general dermatology disability index designed to assess health-related quality of life in adult participants with skin diseases. The measure is widely used: it has been tested across 32 different skin conditions and is available in 55 languages. It is a self-administered questionnaire which includes domains of daily activity, leisure, personal relationships, symptoms and feelings, treatment and school/work activities. Each domain has 4 response categories ranging from 0 (not at all) to 3 (very much). "Not relevant" is a valid score also and is scored as 0. The DLQI total score is a sum of all 10 responses. Scores range from 0 to 30 with higher scores indicating greater health-related quality of life impairment. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

48 and 72 weeks

End point values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg	Secukinumab (AIN457) 150 mg - 300 mg (Maintanence period 1)	Secukinumab (AIN457) 150 mg - 300 mg (Maintenance period 2)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	83	31	16	24
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 48, maintenance 2 (n=79,30,16,24)	-17.2 (± 7.33)	-14.7 (± 6.19)	-11.5 (± 5.98)	-7.7 (± 8.80)
Week 72, maintenance 2 (n=74,26,12,21)	-17.0 (± 7.27)	-13.0 (± 5.62)	-11.3 (± 4.77)	-15.0 (± 8.76)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean EuroQOL 5-Dimension Health Status Questionnaire (EQ-5D) health state assessment scores (from 0 to 100) - Initiation Period

End point title	Mean EuroQOL 5-Dimension Health Status Questionnaire (EQ-5D) health state assessment scores (from 0 to 100) - Initiation Period

End point description:

The EQ-5D is an instrument used to assess a participant's health status. The instrument includes a descriptive profile and a visual analog scale (VAS). The descriptive profile includes 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension had 3 response levels: no problems, some problems and severe problems. The VAS is a vertical scale that assesses the health status from 0 (worst possible health state) to 100 (best possible health state). This outcome measures the percent change in VAS score.

End point type	Secondary

End point timeframe:

12 and 16 weeks

End point values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	115		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12, initiation(n=110,106)	76.25 (± 18.612)	72.92 (± 20.004)		
Week 16, initiation (n=108,103)	76.30 (± 21.580)	75.25 (± 19.100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean EuroQOL 5-Dimension Health Status Questionnaire (EQ-5D) health state assessment scores (from 0 to 100) - Maintenance 1 Period

End point title	Mean EuroQOL 5-Dimension Health Status Questionnaire (EQ-5D) health state assessment scores (from 0 to 100) - Maintenance 1 Period

End point description:

The EQ-5D is an instrument used to assess a participant's health status. The instrument includes a descriptive profile and a visual analog scale (VAS). The descriptive profile includes 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension had 3 response levels: no problems, some problems and severe problems. The VAS is a vertical scale that assesses the health status from 0 (worst possible health state) to 100 (best possible health state). This outcome measures the percent change in VAS score.

End point type	Secondary

End point timeframe:

16, 24 and 48 weeks

End point values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg	Secukinumab (AIN457) 150 mg - 300 mg (Maintanence period 1)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	107	66	37	
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 16, maintenance 1 (n=105,64,37)	77.33 (± 20.665)	80.48 (± 16.099)	67.03 (± 20.657)	
Week 24, maintenance 1 (n=102,64,35)	79.16 (± 18.587)	80.05 (± 16.345)	69.14 (± 19.587)	
Week 48, maintenance 1 (n=86,55,19)	77.73 (± 21.598)	76.07 (± 20.413)	70.37 (± 18.038)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean EuroQOL 5-Dimension Health Status Questionnaire (EQ-5D) health state assessment scores (from 0 to 100) - Maintenance 2 Period

End point title	Mean EuroQOL 5-Dimension Health Status Questionnaire (EQ-5D) health state assessment scores (from 0 to 100) - Maintenance 2 Period

End point description:

The EQ-5D is an instrument used to assess a participant's health status. The instrument includes a descriptive profile and a visual analog scale (VAS). The descriptive profile includes 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension had 3 response levels: no problems, some problems and severe problems. The VAS is a vertical scale that assesses the health status from 0 (worst possible health state) to 100 (best possible health state). This outcome measures the percent change in VAS score.

End point type	Secondary

End point timeframe:
48 and 72 weeks

End point values	Secukinumab (AIN457) 300 mg	Secukinumab (AIN457) 150 mg	Secukinumab (AIN457) 150 mg - 300 mg (Maintanence period 1)	Secukinumab (AIN457) 150 mg - 300 mg (Maintenance period 2)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	83	31	16	24
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 48, maintenance 2 (n=79,30,16,24)	80.22 (± 19.200)	83.87 (± 11.337)	74.50 (± 14.855)	67.63 (± 24.912)
Week 72, maintenance 2 (n=73,26,12,21)	78.24 (± 19.792)	80.88 (± 17.635)	77.67 (± 16.615)	79.67 (± 18.680)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

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	18.0

Reporting groups

Reporting group title	Secukinumab 150mg
Reporting group description:	
Secukinumab 150mg	
Reporting group title	Secukinumab 300mg
Reporting group description:	
Secukinumab 300mg	

Serious adverse events	Secukinumab 150mg	Secukinumab 300mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 115 (12.17%)	24 / 179 (13.41%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Diabetic macroangiopathy			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocution			

subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malaise			
subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Pregnancy of partner			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic specific antigen increased			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Joint injury			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	2 / 115 (1.74%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Alcoholic seizure			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 115 (0.00%)	2 / 179 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug withdrawal convulsions			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hypoaesthesia			
subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic neuritis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 115 (0.87%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pancreatitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 115 (1.74%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis alcoholic			
subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 115 (0.00%)	2 / 179 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash erythematous			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Glomerulonephritis proliferative			

subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriatic arthropathy			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 115 (0.00%)	2 / 179 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lower respiratory tract infection			
subjects affected / exposed	1 / 115 (0.87%)	2 / 179 (1.12%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 115 (1.74%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval abscess			
subjects affected / exposed	1 / 115 (0.87%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			

subjects affected / exposed	0 / 115 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Secukinumab 150mg	Secukinumab 300mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	88 / 115 (76.52%)	152 / 179 (84.92%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 115 (0.00%)	9 / 179 (5.03%)	
occurrences (all)	0	10	
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 115 (6.96%)	7 / 179 (3.91%)	
occurrences (all)	9	7	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	3 / 115 (2.61%)	0 / 179 (0.00%)	
occurrences (all)	3	0	
Fatigue			
subjects affected / exposed	9 / 115 (7.83%)	8 / 179 (4.47%)	
occurrences (all)	28	11	
Influenza like illness			
subjects affected / exposed	8 / 115 (6.96%)	7 / 179 (3.91%)	
occurrences (all)	8	10	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	3 / 115 (2.61%)	6 / 179 (3.35%)	
occurrences (all)	3	6	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 115 (9.57%)	20 / 179 (11.17%)	
occurrences (all)	11	26	

Dyspnoea			
subjects affected / exposed	1 / 115 (0.87%)	4 / 179 (2.23%)	
occurrences (all)	1	4	
Nasal congestion			
subjects affected / exposed	3 / 115 (2.61%)	4 / 179 (2.23%)	
occurrences (all)	3	5	
Oropharyngeal pain			
subjects affected / exposed	9 / 115 (7.83%)	29 / 179 (16.20%)	
occurrences (all)	13	39	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 115 (0.00%)	4 / 179 (2.23%)	
occurrences (all)	0	4	
Psychiatric disorders			
Depression			
subjects affected / exposed	6 / 115 (5.22%)	4 / 179 (2.23%)	
occurrences (all)	7	4	
Insomnia			
subjects affected / exposed	1 / 115 (0.87%)	5 / 179 (2.79%)	
occurrences (all)	1	5	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 115 (1.74%)	6 / 179 (3.35%)	
occurrences (all)	2	6	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 115 (0.87%)	5 / 179 (2.79%)	
occurrences (all)	1	5	
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 115 (2.61%)	6 / 179 (3.35%)	
occurrences (all)	3	7	
Blood glucose increased			
subjects affected / exposed	4 / 115 (3.48%)	3 / 179 (1.68%)	
occurrences (all)	4	4	
Blood triglycerides increased			
subjects affected / exposed	2 / 115 (1.74%)	4 / 179 (2.23%)	
occurrences (all)	3	4	
Gamma-glutamyltransferase			

increased			
subjects affected / exposed	1 / 115 (0.87%)	7 / 179 (3.91%)	
occurrences (all)	1	7	
Lipase increased			
subjects affected / exposed	1 / 115 (0.87%)	6 / 179 (3.35%)	
occurrences (all)	1	6	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 115 (1.74%)	4 / 179 (2.23%)	
occurrences (all)	3	5	
Fall			
subjects affected / exposed	2 / 115 (1.74%)	7 / 179 (3.91%)	
occurrences (all)	2	10	
Joint injury			
subjects affected / exposed	3 / 115 (2.61%)	3 / 179 (1.68%)	
occurrences (all)	3	3	
Limb injury			
subjects affected / exposed	0 / 115 (0.00%)	4 / 179 (2.23%)	
occurrences (all)	0	4	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 115 (1.74%)	9 / 179 (5.03%)	
occurrences (all)	2	9	
Headache			
subjects affected / exposed	27 / 115 (23.48%)	28 / 179 (15.64%)	
occurrences (all)	57	44	
Lethargy			
subjects affected / exposed	3 / 115 (2.61%)	5 / 179 (2.79%)	
occurrences (all)	4	6	
Migraine			
subjects affected / exposed	4 / 115 (3.48%)	2 / 179 (1.12%)	
occurrences (all)	5	3	
Paraesthesia			
subjects affected / exposed	3 / 115 (2.61%)	2 / 179 (1.12%)	
occurrences (all)	4	3	
Eye disorders			

Dry eye			
subjects affected / exposed	3 / 115 (2.61%)	5 / 179 (2.79%)	
occurrences (all)	3	6	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 115 (2.61%)	4 / 179 (2.23%)	
occurrences (all)	3	4	
Abdominal pain upper			
subjects affected / exposed	1 / 115 (0.87%)	5 / 179 (2.79%)	
occurrences (all)	1	6	
Diarrhoea			
subjects affected / exposed	14 / 115 (12.17%)	16 / 179 (8.94%)	
occurrences (all)	17	21	
Dyspepsia			
subjects affected / exposed	7 / 115 (6.09%)	7 / 179 (3.91%)	
occurrences (all)	7	7	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 115 (0.00%)	4 / 179 (2.23%)	
occurrences (all)	0	4	
Mouth ulceration			
subjects affected / exposed	1 / 115 (0.87%)	5 / 179 (2.79%)	
occurrences (all)	1	5	
Nausea			
subjects affected / exposed	2 / 115 (1.74%)	19 / 179 (10.61%)	
occurrences (all)	11	21	
Toothache			
subjects affected / exposed	3 / 115 (2.61%)	2 / 179 (1.12%)	
occurrences (all)	3	6	
Vomiting			
subjects affected / exposed	6 / 115 (5.22%)	12 / 179 (6.70%)	
occurrences (all)	8	12	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	3 / 115 (2.61%)	5 / 179 (2.79%)	
occurrences (all)	4	6	
Hyperhidrosis			

subjects affected / exposed	0 / 115 (0.00%)	4 / 179 (2.23%)	
occurrences (all)	0	4	
Intertrigo			
subjects affected / exposed	3 / 115 (2.61%)	2 / 179 (1.12%)	
occurrences (all)	3	3	
Pruritus			
subjects affected / exposed	3 / 115 (2.61%)	4 / 179 (2.23%)	
occurrences (all)	4	7	
Pruritus generalised			
subjects affected / exposed	3 / 115 (2.61%)	1 / 179 (0.56%)	
occurrences (all)	5	1	
Psoriasis			
subjects affected / exposed	15 / 115 (13.04%)	28 / 179 (15.64%)	
occurrences (all)	17	36	
Rash			
subjects affected / exposed	4 / 115 (3.48%)	6 / 179 (3.35%)	
occurrences (all)	4	7	
Urticaria			
subjects affected / exposed	3 / 115 (2.61%)	1 / 179 (0.56%)	
occurrences (all)	3	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 115 (7.83%)	19 / 179 (10.61%)	
occurrences (all)	16	25	
Arthritis			
subjects affected / exposed	4 / 115 (3.48%)	2 / 179 (1.12%)	
occurrences (all)	4	2	
Back pain			
subjects affected / exposed	8 / 115 (6.96%)	16 / 179 (8.94%)	
occurrences (all)	8	22	
Joint swelling			
subjects affected / exposed	3 / 115 (2.61%)	9 / 179 (5.03%)	
occurrences (all)	3	9	
Musculoskeletal pain			

subjects affected / exposed	4 / 115 (3.48%)	4 / 179 (2.23%)	
occurrences (all)	4	7	
Musculoskeletal stiffness			
subjects affected / exposed	3 / 115 (2.61%)	0 / 179 (0.00%)	
occurrences (all)	4	0	
Myalgia			
subjects affected / exposed	1 / 115 (0.87%)	8 / 179 (4.47%)	
occurrences (all)	2	9	
Neck pain			
subjects affected / exposed	1 / 115 (0.87%)	5 / 179 (2.79%)	
occurrences (all)	2	5	
Pain in extremity			
subjects affected / exposed	3 / 115 (2.61%)	11 / 179 (6.15%)	
occurrences (all)	3	15	
Tendonitis			
subjects affected / exposed	4 / 115 (3.48%)	0 / 179 (0.00%)	
occurrences (all)	4	0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 115 (0.00%)	4 / 179 (2.23%)	
occurrences (all)	0	4	
Conjunctivitis			
subjects affected / exposed	2 / 115 (1.74%)	7 / 179 (3.91%)	
occurrences (all)	3	9	
Ear infection			
subjects affected / exposed	7 / 115 (6.09%)	7 / 179 (3.91%)	
occurrences (all)	10	8	
Folliculitis			
subjects affected / exposed	1 / 115 (0.87%)	4 / 179 (2.23%)	
occurrences (all)	1	4	
Gastroenteritis			
subjects affected / exposed	3 / 115 (2.61%)	3 / 179 (1.68%)	
occurrences (all)	3	3	
Influenza			
subjects affected / exposed	5 / 115 (4.35%)	9 / 179 (5.03%)	
occurrences (all)	5	10	

Lower respiratory tract infection			
subjects affected / exposed	6 / 115 (5.22%)	14 / 179 (7.82%)	
occurrences (all)	7	16	
Nasopharyngitis			
subjects affected / exposed	27 / 115 (23.48%)	52 / 179 (29.05%)	
occurrences (all)	41	69	
Oral candidiasis			
subjects affected / exposed	2 / 115 (1.74%)	7 / 179 (3.91%)	
occurrences (all)	3	12	
Oral herpes			
subjects affected / exposed	6 / 115 (5.22%)	5 / 179 (2.79%)	
occurrences (all)	6	6	
Otitis externa			
subjects affected / exposed	3 / 115 (2.61%)	2 / 179 (1.12%)	
occurrences (all)	5	7	
Pharyngitis			
subjects affected / exposed	1 / 115 (0.87%)	5 / 179 (2.79%)	
occurrences (all)	1	5	
Sinusitis			
subjects affected / exposed	3 / 115 (2.61%)	12 / 179 (6.70%)	
occurrences (all)	3	17	
Tinea pedis			
subjects affected / exposed	1 / 115 (0.87%)	4 / 179 (2.23%)	
occurrences (all)	1	4	
Tonsillitis			
subjects affected / exposed	4 / 115 (3.48%)	3 / 179 (1.68%)	
occurrences (all)	4	3	
Upper respiratory tract infection			
subjects affected / exposed	8 / 115 (6.96%)	9 / 179 (5.03%)	
occurrences (all)	9	9	
Urinary tract infection			
subjects affected / exposed	4 / 115 (3.48%)	10 / 179 (5.59%)	
occurrences (all)	7	14	
Viral upper respiratory tract infection			
subjects affected / exposed	6 / 115 (5.22%)	11 / 179 (6.15%)	
occurrences (all)	13	16	

Vulvovaginal candidiasis			
subjects affected / exposed	6 / 115 (5.22%)	8 / 179 (4.47%)	
occurrences (all)	8	13	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	3 / 115 (2.61%)	0 / 179 (0.00%)	
occurrences (all)	3	0	
Gout			
subjects affected / exposed	3 / 115 (2.61%)	1 / 179 (0.56%)	
occurrences (all)	3	1	
Type 2 diabetes mellitus			
subjects affected / exposed	4 / 115 (3.48%)	2 / 179 (1.12%)	
occurrences (all)	4	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 August 2013	The main purpose of this amendment was that female patients were required to use two effective forms of contraception and male patients were required to use one effective form of contraception
28 November 2013	The main purposes of this amendment were the primary endpoint was changed from 12 weeks to 16 weeks; 12 weeks efficacy was included as a secondary endpoint; the option of up titration at for patients on the 150mg dose secukinumab to 300mg if they were not achieving the NICE criteria; and administrative changes.
03 July 2014	The main purpose of this amendment was to further evaluate: secukinumab safety, efficacy and tolerability for a further 24 weeks; patient response in those patients not achieving adequate efficacy on 150mg secukinumab at Week 48, when up-titrated to 300mg; PASI 50, 75 and 90 response at 24, 48 and 72 weeks; and previous exposure to Ustekinumab no longer an exclusion criteria.
22 February 2016	Minor administrative updates were made to the protocol including: an updated author and steering committee list; minor corrections to the numbering of days for maintenance period 2; Updates to the patient exposure and post-marketing experience information; Update to the use of the results and interim analysis; Clarification on the acceptable duration of concomitant mild-moderate topical steroids; Clarification on prohibited meds; Correction to the description of the statistical model, hypothesis and method of analysis section

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported