Clinical trial results:
A 24-week, multicenter, proSpective stUdy to evaluate the PASI 90 clinical response rate and the safety PRofile of sEcukinuMab 300 mg in Cw6-negativE and Cw6-positive patients with moderate to severe chronic plaque-type psoriasis (SUPREME) – amended with an extension treatment period of up to 48 weeks

Summary

EudraCT number	2014-002865-31
Trial protocol	IT
Global end of trial date	08 June 2017

Results information

Result version number	v1 (current)
This version publication date	23 June 2018
First version publication date	23 June 2018

Trial information

Trial identification

Sponsor protocol code	CAIN457AIT01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02394561
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 41 613241111, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office,, Novartis Pharma AG, 41 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	08 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 June 2017
Global end of trial reached?	Yes
Global end of trial date	08 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the clinical response in Cw6-negative and Cw6-positive patients treated with secukinumab 300 mg with respect to the Psoriasis Area Severity Index (PASI) 90 response rate after 16 weeks, and thereafter for up to 72 weeks

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	10 April 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 431
Worldwide total number of subjects	431
EEA total number of subjects	431

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)	395
From 65 to 84 years	36
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Five hundred thirty participants were screened and 434 entered the CORE Phase. However, there were 3 patients without Cw6 assessment which was necessary for stratification to the two arms, therefore 431 were considered enrolled.

Period 1

Period 1 title	CORE Phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cw6-positive AIN457 300 mg

Arm description:

Stratified to Cw6 positive cohort. Investigators and patients were blinded to Cw6 results. All patients were treated according to an induction regimen of two injections of secukinumab 150 mg a week for five weeks starting at baseline (week 0), followed by a maintenance period of two injections per month. At week 16, patients achieving PASI 50 response were eligible to continue on secukinumab for an additional 8 weeks in CORE. Eligible patients with at least a PASI 75 response were included in the extension phase, up to 72 weeks

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

Dosage and administration details:

two subcutaneous injections secukimumab 150 Mg

Arm title	Cw6-negative AIN457 300 mg

Arm description:

Stratified to Cw6 negative cohort. Investigators and patients were blinded to Cw6 results. All patients were treated according to an induction regimen of two injections of secukinumab 150 mg a week for five weeks starting at baseline (week 0), followed by a maintenance period of two injections per month. At week 16, patients achieving PASI 50 response were eligible to continue on secukinumab for an additional 8 weeks in CORE. Eligible patients with at least a PASI 75 response were included in the extension phase, up to 72 weeks

Arm type	Experimental
Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN587
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

two subcutaneous injections secukimumab 150 Mg

Number of subjects in period 1	Cw6-positive AIN457 300 mg	Cw6-negative AIN457 300 mg
Started	185	246
Full Analysis set	185	246
Safety set	185	246
ITT set	184	246
Completed	172	227
Not completed	13	19
Adverse event, serious fatal	-	1
Physician decision	1	1
Consent withdrawn by subject	2	2
Adverse event, non-fatal	7	9
Pregnancy	1	-
Lost to follow-up	1	-
Lack of efficacy	1	6

Period 2

Period 2 title	Extension Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cw6-positive AIN457 300 mg

Arm description:

Stratified to Cw6 positive cohort. Investigators and patients were blinded to Cw6 results. All patients were treated according to an induction regimen of two injections of secukinumab 150 mg a week for five weeks starting at baseline (week 0), followed by a maintenance period of two injections per month. At week 16, patients achieving PASI 50 response were eligible to continue on secukinumab for an additional 8 weeks in CORE. Eligible patients with at least a PASI 75 response were included in the extension phase, up to 72 weeks

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

Dosage and administration details:

two subcutaneous injections secukimumab 150 Mg

Arm title	Cw6-negative AIN457 300 mg

Arm description:

Stratified to Cw6 negative cohort. Investigators and patients were blinded to Cw6 results. All patients were treated according to an induction regimen of two injections of secukinumab 150 mg a week for five weeks starting at baseline (week 0), followed by a maintenance period of two injections per month. At

week 16, patients achieving PASI 50 response were eligible to continue on secukinumab for an additional 8 weeks in CORE. Eligible patients with at least a PASI 75 response were included in the extension phase, up to 72 weeks

Arm type	Experimental
Investigational medicinal product name	secukinumab
Investigational medicinal product code	AIN587
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

two subcutaneous injections secukimumab 150 Mg

Number of subjects in period 2[1]	Cw6-positive AIN457 300 mg	Cw6-negative AIN457 300 mg
Started	162	219
Completed	151	207
Not completed	11	12
Adverse event, serious fatal	-	1
Physician decision	-	2
Consent withdrawn by subject	-	5
Adverse event, non-fatal	6	1
Lost to follow-up	1	-
Protocol deviation	1	-
Lack of efficacy	3	3

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all patients from the CORE entered the Extension Phase

Baseline characteristics

Reporting groups	
Reporting group title	Cw6-positive AIN457 300 mg
Reporting group description:	
Stratified to Cw6 positive cohort. Investigators and patients were blinded to Cw6 results. All patients were treated according to an induction regimen of two injections of secukinumab 150 mg a week for five weeks starting at baseline (week 0), followed by a maintenance period of two injections per month. At week 16, patients achieving PASI 50 response were eligible to continue on secukinumab for an additional 8 weeks in CORE. Eligible patients with at least a PASI 75 response were included in the extension phase, up to 72 weeks	
Reporting group title	Cw6-negative AIN457 300 mg
Reporting group description:	
Stratified to Cw6 negative cohort. Investigators and patients were blinded to Cw6 results. All patients were treated according to an induction regimen of two injections of secukinumab 150 mg a week for five weeks starting at baseline (week 0), followed by a maintenance period of two injections per month. At week 16, patients achieving PASI 50 response were eligible to continue on secukinumab for an additional 8 weeks in CORE. Eligible patients with at least a PASI 75 response were included in the extension phase, up to 72 weeks	

Reporting group values	Cw6-positive AIN457 300 mg	Cw6-negative AIN457 300 mg	Total
Number of subjects	185	246	431
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)	173	222	395
From 65-84 years	12	24	36
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	42.71	47.18	
standard deviation	± 13.148	± 12.919	-
Sex: Female, Male Units: Subjects			
Female	60	62	122
Male	125	184	309
Race/Ethnicity, Customized Units: Subjects			
Caucasian|	184	241	425
Asian|	0	1	1
Native American|	0	1	1
Unknown|	0	2	2
Other|	1	1	2

Time since first diagnosis of psoriasis Units: years			
arithmetic mean	19.63	17.46	
standard deviation	± 12.489	± 11.343	-

End points

End points reporting groups

Reporting group title	Cw6-positive AIN457 300 mg

Reporting group description:

Stratified to Cw6 positive cohort. Investigators and patients were blinded to Cw6 results. All patients were treated according to an induction regimen of two injections of secukinumab 150 mg a week for five weeks starting at baseline (week 0), followed by a maintenance period of two injections per month. At week 16, patients achieving PASI 50 response were eligible to continue on secukinumab for an additional 8 weeks in CORE. Eligible patients with at least a PASI 75 response were included in the extension phase, up to 72 weeks

Reporting group title	Cw6-negative AIN457 300 mg

Reporting group description:

Stratified to Cw6 negative cohort. Investigators and patients were blinded to Cw6 results. All patients were treated according to an induction regimen of two injections of secukinumab 150 mg a week for five weeks starting at baseline (week 0), followed by a maintenance period of two injections per month. At week 16, patients achieving PASI 50 response were eligible to continue on secukinumab for an additional 8 weeks in CORE. Eligible patients with at least a PASI 75 response were included in the extension phase, up to 72 weeks

Reporting group title	Cw6-positive AIN457 300 mg

Reporting group description:

Stratified to Cw6 positive cohort. Investigators and patients were blinded to Cw6 results. All patients were treated according to an induction regimen of two injections of secukinumab 150 mg a week for five weeks starting at baseline (week 0), followed by a maintenance period of two injections per month. At week 16, patients achieving PASI 50 response were eligible to continue on secukinumab for an additional 8 weeks in CORE. Eligible patients with at least a PASI 75 response were included in the extension phase, up to 72 weeks

Reporting group title	Cw6-negative AIN457 300 mg

Reporting group description:

Stratified to Cw6 negative cohort. Investigators and patients were blinded to Cw6 results. All patients were treated according to an induction regimen of two injections of secukinumab 150 mg a week for five weeks starting at baseline (week 0), followed by a maintenance period of two injections per month. At week 16, patients achieving PASI 50 response were eligible to continue on secukinumab for an additional 8 weeks in CORE. Eligible patients with at least a PASI 75 response were included in the extension phase, up to 72 weeks

Subject analysis set title	Difference in % (Cw6-pos vs Cw6-neg)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Difference in percentages of the two cohorts in IGA 0/1 and PASI 50, 75, 90,100 at all time points.

Subject analysis set title	All Patients
Subject analysis set type	Full analysis

Subject analysis set description:

All patients in the Full Analysis Set.

Subject analysis set title	All Patients
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients in the Safety Set

Primary: Percentage (%) of patients who reach Psoriasis area severity index (PASI) 90 at 16 weeks - LOCF approach (ITT set)

End point title	Percentage (%) of patients who reach Psoriasis area severity index (PASI) 90 at 16 weeks - LOCF approach (ITT set)

End point description:

PASI (Langley et al 2015) combines the assessment of the severity of lesions and the area affected into a single score with a range of 0 (no disease) to 72 (maximal disease). The PASI was assessed at all visits in CORE and extension phases. PASI 90 response: patients achieving ≥ 90% improvement (reduction) in PASI score compared to baseline are defined as PASI 90 responders.

End point type	Primary
End point timeframe:	
Baseline up to 16 weeks	

End point values	Cw6-positive AIN457 300 mg	Cw6-negative AIN457 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	246		
Units: percentage of participants				
number (confidence interval 95%)	80.4 (74.0 to 85.9)	81.7 (76.3 to 86.3)		

Statistical analyses

Statistical analysis title	PASI 90 differencee
Comparison groups	Cw6-positive AIN457 300 mg v Cw6-negative AIN457 300 mg
Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	6.2

Secondary: Percentage (%) of patients with IGA 0/1, PASI 50, PASI 75, PASI 90, PASI 100 responders by visit - LOCF approach (ITT set)

End point title	Percentage (%) of patients with IGA 0/1, PASI 50, PASI 75, PASI 90, PASI 100 responders by visit - LOCF approach (ITT set)
End point description:	
IGA mod 2011 scale measures severity of the psoriasis on a five-point scale ranging from 0 (no disease, 'clear') to 4 ('very severe'). PASI 50,75,90,100 represent: patients achieving ≥ 50% improvement (reduction) in PASI score compared to baseline, ≥ 75% improvement (reduction), ≥ 90% improvement (reduction) and PASI 100 response/remission: complete clearing of psoriasis (PASI=0).	
End point type	Secondary
End point timeframe:	
Baseline up to approximately 72 weeks	

End point values	Cw6-positive AIN457 300 mg	Cw6-negative AIN457 300 mg	Difference in % (Cw6-pos vs Cw6-neg)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	184	246	430	
Units: percentage of participants				
number (confidence interval 95%)				
W1 IGA 0/1 n=178,240,418|	2.2 (0.62 to 5.65)	2.1 (0.68 to 4.79)	0.16 (-2.86 to 3.75)	
W1 PASI 50 n=179,240,419|	13.4 (8.78 to 19.29)	12.1 (8.24 to 16.89)	1.32 (-5.02 to 8.09)	
W1 PASI 75 n=179,240,419|	2.2 (0.61 to 5.62)	0.4 (0.01 to 2.30)	1.82 (-0.52 to 5.20)	
W2 IGA 0/1 n=184,246,430|	8.7 (5.05 to 13.74)	6.9 (4.08 to 10.83)	1.79 (-3.29 to 7.36)	
W2 PASI 50 n=184,245,430|	44.0 (36.73 to 51.51)	44.5 (38.16 to 50.95)	-0.47 (-9.84 to 8.98)	
W2 PASI 75n=184,245,430|	15.8 (10.82 to 21.84)	10.2 (6.71 to 14.69)	5.56 (-0.80 to 12.32)	
W2 PASI 90 n=184,245,430|	3.3 (1.21 to 6.96)	2.4 (0.90 to 5.25)	0.81 (-2.49 to 4.71)	
W2 PASI 100 n=184,245,430|	0.5 (0.01 to 2.99)	0.4 (0.01 to 2.25)	0.14 (-1.78 to 2.63)	
W3 IGA 0/1 n=184,246,430|	24.5 (18.43 to 31.32)	21.1 (16.21 to 26.78)	3.32 (-4.58 to 11.46)	
W3 PASI 50 n=184,245,429|	76.1 (69.26 to 82.06)	71.8 (65.76 to 77.38)	4.25 (-4.23 to 12.40)	
W3 PASI 75 n=184,245,429|	38.6 (31.52 to 46.03)	34.3 (28.36 to 40.60)	4.30 (-4.81 to 13.46)	
W3 PASI 90 n=184,245,429|	13.0 (8.54 to 18.78)	11.4 (7.73 to 16.09)	1.61 (-4.55 to 8.19)	
W3 PASI 100 n=184,245,429|	2.7 (0.89 to 6.23)	2.4 (0.90 to 5.25)	0.27 (-2.92 to 4.00)	
W4 IGA 0/1 n=184,246,430|	42.4 (35.15 to 49.88)	39.8 (33.67 to 46.25)	2.55 (-6.75 to 11.89)	
W4 PASI 50 n=184,246,430|	87.5 (81.84 to 91.91)	87.4 (82.59 to 91.27)	0.10 (-6.51 to 6.31)	
W4 PASI 75 n=184,246,430|	61.4 (53.97 to 68.48)	57.3 (50.88 to 63.58)	4.10 (-5.29 to 13.28)	
W4 PASI 90 n=184,246,430|	27.7 (21.39 to 34.78)	22.0 (16.94 to 27.65)	5.77 (-2.40 to 14.10)	
W4 PASI 100 n=184,246,430|	10.3 (6.33 to 15.66)	9.8 (6.35 to 14.17)	0.57 (-5.09 to 6.66)	
W8 IGA 0/1 n=184,246,430|	72.3 (65.22 to 78.61)	73.2 (67.17 to 78.60)	-0.89 (-9.48 to 7.47)	
W8 PASI 50 n=184,246,430|	95.7 (91.61 to 98.10)	95.1 (91.63 to 97.45)	0.53 (-3.97 to 4.59)	
W8 PASI 75 n=184,246,430|	84.8 (78.76 to 89.64)	85.0 (79.87 to 89.18)	-0.18 (-7.26 to 6.53)	
W8 PASI 90 n=184,246,430|	61.4 (53.97 to 68.48)	60.6 (54.16 to 66.72)	0.84 (-8.46 to 10.01)	
W8 PASI 100 n=184,246,430|	34.8 (27.93 to 42.14)	34.6 (28.63 to 40.86)	0.23 (-8.72 to 9.34)	
WK12 IGA 0/1 n=184,246,430|	81.0 (74.55 to 86.38)	81.7 (76.30 to 86.33)	-0.73 (-8.36 to 6.57)	
WK12 PASI 50 n=184,246,430|	97.3 (93.77 to 99.11)	97.2 (94.23 to 98.85)	0.13 (-3.65 to 3.43)	
WK12 PASI 75 n=184,246,430|	92.9 (88.22 to 96.18)	90.7 (86.30 to 93.98)	2.28 (-3.27 to 7.46)	
WK12 PASI 90 n=184,246,430|	72.8 (65.79 to 79.11)	73.6 (67.60 to 78.98)	-0.75 (-9.30 to 7.56)	

WK12 PASI 100 n=184,246,430|	49.5 (42.02 to 56.91)	43.9 (37.60 to 50.35)	5.55 (-3.93 to 14.94)	
WK16 IGA 0/1 n=184,246,430|	85.3 (79.37 to 90.10)	86.2 (81.23 to 90.23)	-0.85 (-7.79 to 5.70)	
WK16 PASI 50 n=184,246,430|	97.8 (94.53 to 99.40)	98.8 (96.48 to 99.75)	-0.95 (-4.33 to 1.70)	
WK16 PASI 75 n=184,246,430|	94.0 (89.56 to 96.98)	93.1 (89.17 to 95.92)	0.93 (-4.16 to 5.60)	
WK16 PASI 90 n=184,246,430|	80.4 (73.96 to 85.90)	81.7 (76.30 to 86.33)	-1.27 (-8.94 to 6.08)	
WK16 PASI 100 n=184,246,430|	59.2 (51.77 to 66.41)	53.3 (46.81 to 59.62)	5.99 (-3.49 to 15.24)	
WK20 IGA0/1 n=184,246,430|	87.0 (81.22 to 91.46)	87.4 (82.59 to 91.27)	-0.44 (-7.11 to 5.83)	
WK20 PASI 50 n=184,246,430|	97.8 (94.53 to 99.40)	97.6 (94.77 to 99.10)	0.27 (-3.27 to 3.34)	
WK20 PASI 75 n=184,246,430|	94.6 (90.23 to 97.36)	92.7 (88.68 to 95.61)	1.88 (-3.14 to 6.53)	
WK20 PASI 90 n=184,246,430|	81.0 (74.55 to 86.38)	81.7 (76.30 to 86.33)	-0.73 (-8.36 to 6.57)	
WK20 PASI 100 n=184,246,430|	59.8 (52.32 to 66.93)	57.3 (50.88 to 63.58)	2.47 (-6.93 to 11.71)	
WK24 IGA 0/1 n=184,246,430|	89.7 (84.34 to 93.67)	85.4 (80.32 to 89.54)	4.31 (-2.21 to 10.45)	
WK24 PASI 50 n=184,246,430|	97.3 (93.77 to 99.11)	97.2 (94.23 to 98.85)	0.13 (-3.65 to 3.43)	
WK24 PASI 75 n=184,246,430|	94.6 (90.23 to 97.36)	93.1 (89.17 to 95.92)	1.48 (-3.51 to 6.07)	
WK24 PASI 90 n=184,246,430|	84.2 (78.16 to 89.18)	83.3 (78.08 to 87.77)	0.91 (-6.35 to 7.79)	
WK24 PASI 100 n=184,246,430|	62.0 (54.52 to 69.00)	61.4 (54.99 to 67.50)	0.57 (-8.71 to 9.71)	
WK36 IGA 0/1 n=161,219,380|	91.9 (86.59 to 95.63)	90.9 (86.25 to 94.33)	1.06 (-5.06 to 6.68)	
WK36 PASI 50 n=161,219,380|	98.8 (95.58 to 99.85)	99.1 (96.74 to 99.89)	-0.33 (-3.57 to 2.19)	
WK36 PASI 75 n=161,219,380|	94.4 (89.65 to 97.41)	95.0 (91.19 to 97.47)	-0.57 (-5.75 to 4.00)	
WK36 PASI 90n=161,219,380|	88.8 (82.91 to 93.24)	84.0 (78.48 to 88.61)	4.80 (-2.39 to 11.54)	
WK36 PASI 100 n=161,219,380|	65.8 (57.96 to 73.12)	64.4 (57.65 to 70.72)	1.45 (-8.27 to 10.95)	
WK48 IGA 0/1 n=115,159,274|	87.8 (80.42 to 93.18)	86.8 (80.52 to 91.63)	1.03 (-7.43 to 8.82)	
WK48 PASI 50n=115,159,274|	98.3 (93.86 to 99.79)	98.1 (94.59 to 99.61)	0.15 (-4.41 to 3.88)	
WK48 PASI 75 n=115,159,274|	93.9 (87.86 to 97.52)	91.2 (85.67 to 95.10)	2.72 (-4.18 to 8.98)	
WK48 PASI 90 n=115,159,274|	84.3 (76.40 to 90.45)	80.5 (73.48 to 86.35)	3.84 (-5.59 to 12.64)	
WK48 PASI 100 n=115,159,274|	68.7 (59.38 to 77.02)	61.6 (53.60 to 69.23)	7.06 (-4.44 to 18.02)	
WK60 IGA 0/1 n=80,118,198|	87.5 (78.21 to 93.84)	83.9 (76.00 to 90.02)	3.60 (-6.97 to 13.09)	
WK60 PASI 50 n=80,119,199|	96.3 (89.43 to 99.22)	95.0 (89.35 to 98.13)	1.29 (-5.94 to 7.34)	
WK60 PASI 75 n=80,119,199|	90.0 (81.24 to 95.58)	89.9 (83.05 to 94.68)	0.08 (-9.42 to 8.37)	
WK60 PASI 90 n=80,119,199|	82.5 (72.38 to 90.09)	74.8 (66.01 to 82.30)	7.71 (-4.27 to 18.58)	
WK60 PASI 100 n=80,119,199|	65.0 (53.52 to 75.33)	56.3 (46.91 to 65.37)	8.70 (-5.19 to 21.80)	

WK72 IGA 0/1 n=41,60,101|	85.4 (70.83 to 94.43)	80.0 (67.67 to 89.22)	5.37 (-10.7 to 19.47)	
WK72 PASI 50 n=41,61,102|	92.7 (80.08 to 98.46)	93.4 (84.05 to 98.18)	-0.76 (-13.5 to 9.55)	
WK72 PASI 75 n=41,61,102|	85.4 (70.83 to 94.43)	88.5 (77.78 to 95.26)	-3.16 (-18.1 to 9.79)	
WK72 PASI 90 n=41,61,102|	75.6 (59.70 to 87.64)	73.8 (60.93 to 84.20)	1.84 (-15.8 to 17.98)	
WK72 PASI 100 n=41,61,102|	58.5 (42.11 to 73.68)	50.8 (37.70 to 63.86)	7.72 (-11.7 to 26.08)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent mean changes from baseline in IGA mod 2011 between cohorts at each time point (LOCF) (ITT)

End point title	Percent mean changes from baseline in IGA mod 2011 between cohorts at each time point (LOCF) (ITT)

End point description:

IGA mod 2011 scale measures severity of the psoriasis on a five-point scale ranging from 0 (no disease, 'clear') to 4 ('very severe').

End point type	Secondary

End point timeframe:

Baseline up to approximately 72 weeks

End point values	Cw6-positive AIN457 300 mg	Cw6-negative AIN457 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	246		
Units: numbers on a score				
arithmetic mean (standard deviation)				
W1 n=178,240|	-8.5 (± 16.08)	-7.3 (± 17.04)		
W2 n=184,246|	-22.4 (± 22.73)	-21.6 (± 22.72)		
W3 n=184,246|	-38.0 (± 25.45)	-36.5 (± 27.20)		
W4 n=184,246|	-49.6 (± 29.36)	-49.5 (± 29.24)		
W8 n=184,246|	-71.2 (± 28.60)	-71.2 (± 28.91)		
W12 n=184,246|	-78.7 (± 27.31)	-79.0 (± 25.37)		
W16 n=184,246|	-84.1 (± 24.52)	-83.3 (± 22.97)		
W20 n=184,246|	-85.3 (± 24.26)	-84.5 (± 23.80)		
W24 n=184,246|	-86.2 (± 25.17)	-84.1 (± 26.34)		
W36 n=161,219|	-88.6 (± 22.34)	-87.6 (± 23.82)		

W48 n=115,159|	-86.2 (± 25.75)	-84.9 (± 26.06)		
W60 n=80,118|	-83.3 (± 28.44)	-81.0 (± 26.97)		
W72 n=41,60|	-79.1 (± 32.92)	-75.8 (± 29.58)		

Statistical analyses

No statistical analyses for this end point

Secondary: Median time to reach PASI 90 and 75 (ITT)

End point title	Median time to reach PASI 90 and 75 (ITT)
End point description: Time in days to reach PASI scores of 90 and 75.	
End point type	Secondary
End point timeframe: Baseline up to approximately 72 weeks	

End point values	Cw6-positive AIN457 300 mg	Cw6-negative AIN457 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	246		
Units: days				
PASI 90|	57	58		
PASI 75|	29	29		

Statistical analyses

Statistical analysis title	Difference in PASI 90
Comparison groups	Cw6-positive AIN457 300 mg v Cw6-negative AIN457 300 mg
Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1295
Method	Logrank

Statistical analysis title	Difference in PASI 75
Comparison groups	Cw6-positive AIN457 300 mg v Cw6-negative AIN457 300 mg

Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.447 [1]
Method	Logrank

Notes:

[1] - difference between cohorts for PASI 75 using Kaplan-Meier estimate

Secondary: Change from baseline in the Dermatology Life Quality Index (DLQI) (LOCF) (FAS)

End point title	Change from baseline in the Dermatology Life Quality Index (DLQI) (LOCF) (FAS)

End point description:

The DLQI total score was calculated by summing the score of each domain resulting in a maximum of 30 and a minimum of 0. The higher the score, the more Quality of Life was impaired. Meaning of DLQI Scores: 0-1 = no effect at all on patient's life, 2-5 = small effect on patient's life, 6- 10 = moderate effect on patient's life, 11-20= very large effect on patient's life, 21-30 = extremely large effect on patient's life.

End point type	Secondary

End point timeframe:

Baseline up to approximatly 72 weeks

End point values	All Patients			
Subject group type	Subject analysis set			
Number of subjects analysed	431			
Units: numbers in a score				
arithmetic mean (standard deviation)				
Week 16 n=386|	-8.5 (± 6.79)			
Week 24 n=420|	-8.8 (± 7.05)			
Week 48 n=384|	-8.9 (± 7.13)			
Week 72 n=215|	-8.3 (± 6.70)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mean scores of HAD-A and HAD-D (anxiety and depression) (LOCF) (FAS)

End point title	Change from baseline in mean scores of HAD-A and HAD-D (anxiety and depression) (LOCF) (FAS)

End point description:

The Hospital Anxiety and Depression Scale (HADS) is a fourteen-item scale.. Seven of the items relate to anxiety and seven relate to depression. This outcome measure was specifically developed to avoid reliance on aspects of these conditions that are also common somatic symptoms of illness, for example fatigue and insomnia or hypersomnia. Calculations of scores: each of the 14 items was rated on a 4-point scale ('Yes, definitely', 'Yes, sometimes', 'No, not much' and 'No, not at all'). All items except 7 and 10 were scored as 'Yes, definitely' = 3 to 'No, not at all' = 0. Items 7 and 10 were scored as 'Yes, definitely' = 0 to 'No, not at all' = 3. The HADS consisted of two sub-scores: the HAD-A for anxiety and HAD-D for depression; each sub-score ranged from 0 to 21 points; scores ≥11 indicated the presence of anxious or depressive disorders; scores between 8-10 points were borderline abnormal, and scores of

≤7 indicated that the disorder was not present. HADS questionnaire

End point type	Secondary

End point timeframe:

Baseline up approximately 72 weeks

End point values	All Patients			
Subject group type	Subject analysis set			
Number of subjects analysed	431			
Units: numbers on a scale				
arithmetic mean (standard deviation)				
W16 Anxiety n=388|	-1.7 (± 3.37)			
W24 Anxiety n=420|	-2.0 (± 3.38)			
W48 Anxiety n=384|	-2.5 (± 3.67)			
W72 Anxiety n=214|	-2.3 (± 3.44)			
W16 Depression n=388|	-1.3 (± 3.19)			
W24 Depression n=420|	-1.4 (± 3.22)			
W48 Depression n=384|	-1.5 (± 3.31)			
W72 Depression n=214|	-1.7 (± 3.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between the Hospital Anxiety and Depression Scale (HADS) and PASI (FAS)

End point title	Correlation between the Hospital Anxiety and Depression Scale (HADS) and PASI (FAS)

End point description:

PASI score, HADS questionnaire correlation using Spearman rank correlation coefficient

End point type	Secondary

End point timeframe:

Baseline up to approximately 72 weeks

End point values	All Patients			
Subject group type	Subject analysis set			
Number of subjects analysed	431			
Units: numbers on scores				
Baseline|	2			
Week 16|	19			
Week 24|	18			
Week 48|	21			
Week 72|	32			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in Body Mass Index (Safety Set)

End point title	Changes from baseline in Body Mass Index (Safety Set)

End point description:

Change in Body mass index from baseline for patients with a value at baseline and the respective post-baseline visit

End point type	Secondary

End point timeframe:

Baseline up to approximately 72 weeks

End point values	Cw6-positive AIN457 300 mg	Cw6-negative AIN457 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	246		
Units: kg/m2				
arithmetic mean (standard deviation)				
Week 16 n=163,224|	-0.064 (± 0.7748)	-0.047 (± 0.9905)		
Week 24 n=170,231|	0.086 (± 1.0213)	-0.071 (± 1.2260)		
Week 48 n=103,141|	0.302 (± 1.3474)	-0.052 (± 1.4991)		
Week 72 n=29,46|	0.533 (± 1.8101)	-0.015 (± 1.8982)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in Waist Circumference (Safety Set)

End point title	Changes from baseline in Waist Circumference (Safety Set)

End point description:

Change in waist circumference from baseline for patients with a value at baseline and the respective post-baseline visit

End point type	Secondary

End point timeframe:

Baseline up to approximately 72 weeks

End point values	Cw6-positive AIN457 300 mg	Cw6-negative AIN457 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	246		
Units: cm				
arithmetic mean (standard deviation)				
Week 16 n=153,210|	-0.86 (± 3.147)	-0.40 (± 3.006)		
Week 24 n=154,216|	-0.81 (± 3.689)	-0.73 (± 4.119)		
Week 48 n=95,131|	-0.76 (± 4.596)	-0.72 (± 5.547)		
Week 72 n=27,43|	-1.81 (± 4.583)	-0.47 (± 4.501)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline in Weight (Safety Set)

End point title	Changes from baseline in Weight (Safety Set)

End point description:

Change in weight from baseline for patients with a value at baseline and the respective post-baseline visit

End point type	Secondary

End point timeframe:

Baseline up to approximately 72 weeks

End point values	Cw6-positive AIN457 300 mg	Cw6-negative AIN457 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	246		
Units: kg				
arithmetic mean (standard deviation)				
Week 16 n163,224|	-0.20 (± 2.242)	-0.13 (± 2.809)		
Week 24 n=170,231|	0.24 (± 3.008)	-0.21 (± 3.572)		
Week 48 n=103,141|	0.87 (± 3.909)	-0.15 (± 4.329)		
Week 72 n=29,46|	1.40 (± 4.678)	-0.05 (± 5.538)		

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 are reported in this record from First Patient First Treatment until Last Patient Last Visit up to approximately 72 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	20.0

Reporting groups

Reporting group title	Cw6-Positive AIN457 300 mg

Reporting group description:

Cw6-Positive AIN457 300 mg

Reporting group title	Cw6-Negative AIN457 300 mg

Reporting group description:

Cw6-Negative AIN457 300 mg

Serious adverse events	Cw6-Positive AIN457 300 mg	Cw6-Negative AIN457 300 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 185 (5.41%)	21 / 246 (8.54%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 185 (0.54%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 185 (0.54%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma in situ			

subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
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			
Asthenia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
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 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Scrotal inflammation			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			
subjects affected / exposed	1 / 185 (0.54%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal pain			

subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract irritation			
subjects affected / exposed	1 / 185 (0.54%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 185 (0.54%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 185 (0.00%)	2 / 246 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 185 (0.54%)	2 / 246 (0.81%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	1 / 185 (0.54%)	2 / 246 (0.81%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neutropenia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 185 (0.54%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic lesion			

subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 185 (0.00%)	3 / 246 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertransaminasaemia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 246 (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			
Proteinuria			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enthesopathy			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscal degeneration			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteoarthritis			
subjects affected / exposed	0 / 185 (0.00%)	1 / 246 (0.41%)	
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 / 185 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			
subjects affected / exposed	1 / 185 (0.54%)	0 / 246 (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 / 185 (0.54%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	1 / 185 (0.54%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cw6-Positive AIN457 300 mg	Cw6-Negative AIN457 300 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 185 (10.81%)	14 / 246 (5.69%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 185 (5.95%)	10 / 246 (4.07%)	
occurrences (all)	15	10	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	12 / 185 (6.49%)	4 / 246 (1.63%)	
occurrences (all)	16	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2014	The primary objective of the study was reworded: "To evaluate the clinical response in Cw6-negative patients compared to Cw6-positive patients treated with secukinumab 300 mg with respect to the PASI 90 response rate after 16 weeks". Other parts of the protocol, as well as the description of the study rational, were also modified to suit the aim of the study. Population was stratified for different variables that could condition therapeutic response, and appropriately identified TNF-α polymorphism, smoking, BMI and metabolic syndrome. Other items were also corrected or clarified in this amendment: better defined inclusion criteria concerning the psoriasis diagnosis, differentiated the wash-out periods to be used for biological immunomodulating agents before starting treatment with secukinumab, specified the hepatitis B surface antigens and antibodies used for required hepatitis B testing, removed FPG and lipid panel from the "fasting lab assessments", clarified the number of injections of secukinumab to be administered during the treatment period,
03 September 2015	This amendment was to provide continued treatment of patients on secukinumab for an additional 48 weeks (overall up to 72 weeks), and thus allowed for safety, tolerability, and efficacy data collection from the participating patients over a longer period of time. Furthermore, as a consequence of the European Medicines Agency's (EMA) approval in February 2015 of secukinumab "for the treatment of moderate severe plaque psoriasis in adults who are candidates for systemic therapy," inclusion criterion number 5 was changed in order to guarantee treatment to the population of systemically naïve patients, as per label.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported