



## 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 |
|------------------------------|-----|

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | 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 secukinumab 150 Mg

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | 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 secukinumab 150 Mg

| <b>Number of subjects in period 1</b> | Cw6-positive<br>AIN457 300 mg | Cw6-negative<br>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                        |
| <b>Arm title</b>             | 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 secukinumab 150 Mg

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | 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 secukinumab 150 Mg

| <b>Number of subjects in period 2<sup>[1]</sup></b> | Cw6-positive<br>AIN457 300 mg | Cw6-negative<br>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<br>AIN457 300 mg | Cw6-negative<br>AIN457 300 mg | Total |
|---|-------------------------------|-------------------------------|-------|
| Number of subjects                                    | 185                           | 246                           | 431   |
| Age categorical<br>Units: Subjects                    |                               |                               |       |
| In utero  | 0                             | 0                             | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0                             | 0                             | 0     |
| Newborns (0-27 days)                                  | 0                             | 0                             | 0     |
| Infants and toddlers (28 days-23<br>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<br>Units: years                        |                               |                               |       |
| arithmetic mean                                       | 42.71                         | 47.18                         |       |
| standard deviation                                    | ± 13.148                      | ± 12.919                      | -     |
| Sex: Female, Male<br>Units: Subjects                  |                               |                               |       |
| Female  | 60                            | 62                            | 122   |
| Male  | 125                           | 184                           | 309   |
| Race/Ethnicity, Customized<br>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                      | $\pm 12.489$ | $\pm 11.343$ | - |

## 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  $\geq 90\%$  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<br>AIN457 300<br>mg | Cw6-negative<br>AIN457 300<br>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 $\geq 50\%$ improvement (reduction) in PASI score compared to baseline, $\geq 75\%$ improvement (reduction), $\geq 90\%$ 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<br>AIN457 300<br>mg | Cw6-negative<br>AIN457 300<br>mg | Difference in %<br>(Cw6-pos vs<br>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<br>AIN457 300<br>mg | Cw6-negative<br>AIN457 300<br>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 (±<br>25.75) | -84.9 (±<br>26.06) |  |  |
| W60 n=80,118  | -83.3 (±<br>28.44) | -81.0 (±<br>26.97) |  |  |
| W72 n=41,60   | -79.1 (±<br>32.92) | -75.8 (±<br>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:<br>Time in days to reach PASI scores of 90 and 75. |   |
| End point type  | Secondary                                 |
| End point timeframe:<br>Baseline up to approximately 72 weeks             |   |

| End point values            | Cw6-positive<br>AIN457 300<br>mg | Cw6-negative<br>AIN457 300<br>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

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | 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   |

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | 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 <sup>[1]</sup> |
| 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 approximately 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<br>AIN457 300<br>mg | Cw6-negative<br>AIN457 300<br>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 (±<br>0.7748)             | -0.047 (±<br>0.9905)             |  |  |
| Week 24 n=170,231                    | 0.086 (±<br>1.0213)              | -0.071 (±<br>1.2260)             |  |  |
| Week 48 n=103,141                    | 0.302 (±<br>1.3474)              | -0.052 (±<br>1.4991)             |  |  |
| Week 72 n=29,46                      | 0.533 (±<br>1.8101)              | -0.015 (±<br>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<br>AIN457 300<br>mg | Cw6-negative<br>AIN457 300<br>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 (±<br>3.147)               | -0.40 (±<br>3.006)               |  |  |
| Week 24 n=154,216                    | -0.81 (±<br>3.689)               | -0.73 (±<br>4.119)               |  |  |
| Week 48 n=95,131                     | -0.76 (±<br>4.596)               | -0.72 (±<br>5.547)               |  |  |
| Week 72 n=27,43                      | -1.81 (±<br>4.583)               | -0.47 (±<br>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<br>AIN457 300<br>mg | Cw6-negative<br>AIN457 300<br>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 (±<br>2.242)               | -0.13 (±<br>2.809)               |  |  |
| Week 24 n=170,231                    | 0.24 (± 3.008)                   | -0.21 (±<br>3.572)               |  |  |
| Week 48 n=103,141                    | 0.87 (± 3.909)                   | -0.15 (±<br>4.329)               |  |  |
| Week 72 n=29,46                      | 1.40 (± 4.678)                   | -0.05 (±<br>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<br>AIN457 300 mg | Cw6-Negative<br>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 %



| <b>Non-serious adverse events</b>                     | Cw6-Positive<br>AIN457 300 mg | Cw6-Negative<br>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 rationale, 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- $\alpha$ 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