NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

secukinumab

Trial Indication

Plaque psoriasis

Protocol Number

CAIN457AUS07

Protocol Title

A randomized, double-blind, placebo-controlled, parallel-group, multicenter study to explore changes in subcutaneous adipose tissue and modulation of skin inflammation after 12 weeks of treatment with secukinumab, compared to placebo, and up to 52 weeks of treatment with secukinumab in adult patients with moderate to severe plaque psoriasis

Clinical Trial Phase

Phase 4

Phase of Drug Development

Phase IV

Study Start/End Dates

Study Start Date: April 2017
Primary Completion Date: April 2018
Study Completion Date: February 2019

Study Design/Methodology

This was a randomized, double-blind, placebo-controlled, multicenter design. Patients with moderate to severe plaque psoriasis received secukinumab 300 mg or placebo, with randomization stratified by body weight (< 90 kg, ≥ 90 kg). There were 5 periods to the study: Screening (1 to 4 weeks), Double-blind Treatment Period (12 weeks), Double-blind Induction Period (4 weeks), Open-label. Treatment Period (36 weeks), and Follow-up Period (1 week).

During the Double-blind Treatment Period, all patients attended study visits at Baseline, Weeks 1, 2, 3, 4, 8, and 12, and all doses of study treatment were self-administered at the study site. Patients underwent lesional (LS) and non-lesional (NL) skin biopsies at Baseline and Week 12. Assessments for the primary efficacy variable were performed at Week 12 before patients received their Week 12 dose.

During the Double-blind Induction Period, patients randomized to placebo were switched to secukinumab 300 mg for the remainder of the study.

K16 and skin histology/biomarkers were assessed from skin biopsies. The Psoriasis Assessment and Severity Index (PASI) and the Investigator's Global Assessment modified 2011 scale (IGA mod 2011) were performed at specified study visits. Safety was monitored by vital signs, weight, waist circumference, body mass index (BMI), and clinical laboratory tests (serum chemistry, hematology, highsensitivity C-reactive protein (hs-CRP), hemoglobin A1c (HbA1c), homeostatic assessment of insulin resistance (HOMA-IR), viral serology, serum and urine pregnancy).

Centers

United States (16)

Objectives

Primary Objective

To explore the modulation of subcutaneous (s.c.) adipose tissue and skin inflammation from Baseline to Week 12 in patients with moderate to severe plaque psoriasis treated with secukinumab compared to placebo

Endpoints for the primary objective are:

- Response of psoriasis skin lesions to treatment as measured by:

  a. Response in skin histology/keratin 16 (K16) expression to treatment (yes, no)

  b. Psoriasis Area and Severity Index (PASI) 90 (yes, no)

Secondary Objectives

- To explore changes in biometric measurements from Baseline to Week 12 in patients with moderate to severe plaque psoriasis treated with secukinumab compared to placebo

- To explore the modulation of s.c. adipose tissue and skin inflammation from Baseline to Week 52 in patients with moderate to severe plaque psoriasis treated with secukinumab

Endpoints for secondary objectives are:

- Vital signs (blood pressure (BP), weight, waist circumference, BMI), clinical laboratory variables (glucose, insulin, highsensitivity C-reactive protein (hs-CRP), homeostatic model assessment of insulin resistance (HOMA-IR), hemoglobin A1c (HbA1c))

- Response of psoriasis skin lesions to treatment as measured by:

  a. Response in skin histology/K16 expression to treatment (yes, no)

  b. PASI 90 (yes, no)

Test Products, Doses, and Mode of Administration

Secukinumab 300 mg: 1 ml liquid formulation in a 150 mg, single-use prefilled syringe for s.c. injection.

Two syringes were administered at each dose to equal 300 mg secukinumab. Secukinumab was administered once weekly for 5 weeks (at Baseline, Weeks 1, 2, 3, and 4), followed by dosing every 4 weeks, starting at Week 8 through Week 48.
Batch number: S0025.

Placebo: 1 ml liquid formulation in a single-use prefilled syringe for sc injection. Two syringes were administered to simulate the secukinumab dose in order to maintain the blind. Placebo was given once weekly for 5 weeks (at Baseline, Weeks 1, 2, 3, and 4), followed by a dose after 4 weeks at Week 8.

Batch number: 2014485.

Statistical Methods

The data from all centers that participated in this protocol were combined, so that an adequate number of patients were available for analysis. The analysis was conducted on all patient data at the end of Week 12, and at the time the trial ended at Week 52.

The following analysis sets were used for the statistical reporting and analyses:

- Randomized Set: The Randomized Set includes all randomized patients.
- Safety Set: The Safety Set includes all patients who received at least 1 dose of study medication. Patients were included in the analysis according to treatment received.
- Full Analysis Set: The Full Analysis Set comprises all patients to whom study medication had been assigned. Patients inappropriately randomized (eg, Interactive Response Technology was called in error for randomization of a screen failed patient) were excluded from this analysis set.

Concomitant medications were summarized by treatment using frequency counts and percentages for the Safety Set.

Efficacy, safety, and other data were summarized for all weeks up to Week 52.

The primary efficacy variables were response of psoriasis skin lesions to treatment, as measured by:

a. Response in skin histology/K16 expression to treatment (yes, no)
b. PASI 90 (yes, no)

The primary analysis time point was at Week 12.

For the 2 primary efficacy variables at each time point (response in skin histology/K16 expression to treatment at Week 12, PASI 90 at Weeks 4, 8, and 12), 95% confidence intervals for the difference between the 2 treatment groups with respect to the percentage of patients who had the “event” was calculated using the normal approximation to the binomial distribution.

For the two primary efficacy variables at Week 12 (and other time points), a patient with a missing assessment was considered as a nonresponder. Analyses of the primary efficacy variables were based on the Full Analysis Set.

Cross-classification tables of response in skin histology/K16 expression to treatment (yes, no) and response of skin biopsy to treatment (molecular disease pathways) (yes, no), and each of PASI 75, PASI 90, PASI 100, and IGA mod 2011 score of 0 or 1 was provided at Weeks 12, 24, and 52.

The assessment of safety was based mainly on the frequency of AEs and laboratory data. Other safety data, including vital signs (weight, blood pressure, waist circumference, BMI), and clinical laboratory variables (glucose, insulin, hs-CRP, HOMA-IR, HbA1c) were summarized, as appropriate. Analysis of safety data were based on the Safety Set.

The table below considers total sample sizes of 75 patients (50 in secukinumab group and 25 in placebo group) and 99 patients (66 in secukinumab group and 33 in placebo group) to estimate the difference between the 2 groups with respect to the pooled estimate of the 2 percentages of patients who have the “event” at Week 12 for each of the 2 primary efficacy variables. The entries in the table are the “margin of error” (half-width of confidence interval) for a 2-sided 95% confidence interval.

Percentage with “event”	Half-width of confidence interval for n = 75	Half-width of confidence interval for n = 99
30%	25.0%	21.4%
40%	26.5%	22.7%
50%	27.0%	23.2%
60%	26.5%	22.7%
70%	25.0%	21.4%

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Written informed consent must be obtained before any assessment is performed
- Clinical diagnosis of chronic plaque-type psoriasis at least 6 months prior to randomization
- Moderate to severe plaque psoriasis as defined at baseline by:
  - ≥10% Body Surface Area (BSA) involvement and
  - PASI total score of ≥12 and
  - IGA mod 2011 score of ≥3 (based on a scale of 0-4)

Exclusion Criteria:

- Forms of diagnosed psoriasis other than chronic plaque psoriasis
- Medication-induced or medication exacerbated psoriasis
- Previous exposure to secukinumab or any other biologic drug directly targeting IL-17A or IL-17RA receptors
- Ongoing use of prohibited treatments
- Pregnant or nursing (lactating) women

Other protocol-defined inclusion/exclusion criteria may apply.

Participant Flow Table

Overall Study

	Secukinumab 300 mg	Placebo/Secukinumab 300 mg	Total
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization and were started on secukinumab 300 mg at Week 12	
Started	54	28	82
Completed	44	27	71
Not Completed	10	1	11
Lost to Follow-up	6	0	6
Physician Decision	2	0	2

Withdrawal by Subject	1	0	1
Adverse Event	0	1	1
Non-compliance with study treatment	1	0	1

Baseline Characteristics

	Secukinumab 300 mg	Placebo	Total
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization	
Number of Participants [units: participants]	54	28	82
Age Continuous (units: years) Mean ± Standard Deviation			
	41.5±15.20	50.4±13.10	44.5±15.04
Sex: Female, Male[1] (units:) Count of Participants			
Female	22	8	30
Male	32	20	52
Race/Ethnicity, Customized (units:) Count of Participants			
Native American	1	1	2
Unknown	1	0	1
Caucasian	44	19	63

Black	4	4	8
Asian	3	3	6
Other	1	1	2

[1] Count of participants

Summary of Efficacy

Primary Outcome Results

Number and percentage of participants with response of psoriasis skin lesions to treatment at Week 12

(Time Frame: 12 weeks)

	Secukinumab 300 mg	Placebo
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization
Number of Participants Analyzed [units: participants]	54	28
Number and percentage of participants with response of psoriasis skin lesions to treatment at Week 12 (units: participants) Count of Participants		
Week 12	43	1

Statistical Analysis

Groups	Secukinumab 300 mg, Placebo	
Non-Inferiority/Equivalence Test	Other	Statistical hypothesis tests were not performed in this study

Method	Other 95% confidence interval	Statistical analysis of “no” response of skin histology/K16 expression to treatment at Week 12
Other difference in percentages	76.1	
95% Confidence Interval 2-Sided	63.3 to 88.8	

Number of and percentage of participants who achieved Psoriasis Area and Severity Index 90 (PASI 90) at Week 12

(Time Frame: 12 weeks)

	Secukinumab 300 mg	**Placebo**
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization
Number of Participants Analyzed [units: participants]	54	28
Number of and percentage of participants who achieved Psoriasis Area and Severity Index 90 (PASI 90) at Week 12 (units: participants) Count of Participants		
Week 12	29	0

Statistical Analysis

Groups	Secukinumab 300 mg, Placebo	
Non-Inferiority/Equivalence Test	Other	Statistical hypothesis tests were not performed in this study
Method	Other 95% confidence interval	
Other difference in percentages	55.8	
95 % Confidence Interval 2-Sided	42.3 to 69.3	

Secondary Outcome Results

Number and percentage of participants with response of psoriasis skin lesions to treatment at Week 52

(Time Frame: 52 weeks)

	Secukinumab 300 mg	Placebo/Secukinumab 300 mg
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization and were started on secukinumab 300 mg at Week 12
Number of Participants Analyzed [units: participants]	54	28
Number and percentage of participants with response of psoriasis skin lesions to treatment at Week 52 (units: participants) Count of Participants		
Week 52	33	20

Number of and percentage of participants who achieved Psoriasis Area and Severity Index 90 (PASI 90) at Week 52

(Time Frame: 52 weeks)

	Secukinumab 300 mg	Placebo/Secukinumab 300 mg
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization and were started on secukinumab 300 mg at Week 12
Number of Participants Analyzed [units: participants]	54	28
Number of and percentage of participants who achieved Psoriasis Area and Severity Index 90 (PASI 90) at Week 52 (units: participants) Count of Participants		
Week 52	31	20

Change in Systolic Blood Pressure from baseline to Week 12

(Time Frame: baseline, Week 12)

	Secukinumab 300 mg	Placebo
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization
Number of Participants Analyzed [units: participants]	54	28
Change in Systolic Blood Pressure from baseline to Week 12 (units: mmHg) Mean ± Standard Deviation		
	-2.6 ± 11.05	-1.5 ± 11.43

Change in Diastolic Blood Pressure from baseline to Week 12

(Time Frame: baseline, Week 12)

	Secukinumab 300 mg	Placebo
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization
Number of Participants Analyzed [units: participants]	54	28
Change in Diastolic Blood Pressure from baseline to Week 12 (units: mmHg) Mean ± Standard Deviation		
	-0.5 ± 7.92	-0.2 ± 6.18

Change in Body Weight from baseline to Week 12

(Time Frame: baseline, Week 12)

	Secukinumab 300 mg	Placebo
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization
Number of Participants Analyzed [units: participants]	54	28
Change in Body Weight from baseline to Week 12 (units: kg) Mean ± Standard Deviation		
	0.340 ± 2.5475	0.096 ± 3.8729

Change in Glucose level from baseline to Week 12

(Time Frame: baseline, Week 12)

	Secukinumab 300 mg	Placebo
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization
Number of Participants Analyzed [units: participants]	54	28
Change in Glucose level from baseline to Week 12 (units: mmol/L) Mean ± Standard Deviation		
	0.027 ± 0.7505	0.332 ± 1.2933

Change in Insulin level from baseline to Week 12

(Time Frame: baseline, Week 12)

	Secukinumab 300 mg	Placebo
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization
Number of Participants Analyzed [units: participants]	54	28
Change in Insulin level from baseline to Week 12 (units: pmol/L) Mean ± Standard Deviation	15.037 ± 146.6361	141.035 ± 446.2800

Change in High-sensitivity C-reactive Protein (hsCRP) from baseline to Week 12

(Time Frame: baseline, Week 12)

	Secukinumab 300 mg	Placebo
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization
Number of Participants Analyzed [units: participants]	54	28
Change in High-sensitivity C-reactive Protein (hsCRP) from baseline to Week 12 (units: mg/L) Mean ± Standard Deviation	-5.010 ± 24.1279	-1.273 ± 7.6405

Change in Homeostatic Model Assess of Insulin Resistance (UNIT) (HOMA-IR) from baseline to Week 12

(Time Frame: baseline, Week 12)

	Secukinumab 300 mg	Placebo
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization
Number of Participants Analyzed [units: participants]	54	28
Change in Homeostatic Model Assess of Insulin Resistance (UNIT) (HOMA-IR) from baseline to Week 12 (units: scores) Mean ± Standard Deviation		
	0.620 ± 6.0125	7.646 ± 26.5633

Change in Hemoglobin A1c (HbA1c) Test for Diabetes score from baseline to Week 12

(Time Frame: baseline, Week 12)

	Secukinumab 300 mg	Placebo
Arm/Group Description	Participants received secukinumab 300 mg s.c. at randomization	Participants received placebo at randomization
Number of Participants Analyzed [units: participants]	54	28
Change in Hemoglobin A1c (HbA1c) Test for Diabetes score from baseline to Week 12 (units: scores) Mean ± Standard Deviation		
	0.018 ± 0.1889	0.014 ± 0.2138

Summary of Safety

Safety Results

All-Cause Mortality

	Secukinumab 300 mg N = 54	Placebo/Secukinumab 300 mg N = 28
Arm/Group Description	Secukinumab 300 mg	Participants received placebo at randomization and were started on secukinumab 300 mg at Week 12
Total participants affected	0 (0.00%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	Up to 52 weeks
Additional Description	An adverse event (AE) is any sign or symptom that occurs during the study treatment
Source Vocabulary for Table Default	MedDRA (21.0)
Assessment Type for Table Default	Systematic Assessment

	Secukinumab 300 mg N = 54	Placebo/Secukinumab 300 mg N = 28
Arm/Group Description	Secukinumab 300 mg	Participants received placebo at randomization and were started on secukinumab 300 mg at Week 12
Total participants affected	1 (1.85%)	1 (3.57%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		

Testis cancer	0 (0.00%)	1 (3.57%)
Psychiatric disorders		
Suicidal ideation	1 (1.85%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	Up to 52 weeks
Additional Description	An adverse event (AE) is any sign or symptom that occurs during the study treatment
Source Vocabulary for Table Default	MedDRA (21.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	0%

	Secukinumab 300 mg N = 54	**Placebo/Secukinumab 300 mg N = 28**
Arm/Group Description	Secukinumab 300 mg	Participants received placebo at randomization and were started on secukinumab 300 mg at Week 12
Total participants affected	39 (72.22%)	25 (89.29%)
Blood and lymphatic system disorders		
Anaemia	1 (1.85%)	0 (0.00%)
Leukocytosis	0 (0.00%)	1 (3.57%)
Thrombocytosis	0 (0.00%)	1 (3.57%)
Cardiac disorders		
Angina pectoris	0 (0.00%)	1 (3.57%)
Palpitations	1 (1.85%)	0 (0.00%)

Ear and labyrinth disorders		
Ear discomfort	1 (1.85%)	0 (0.00%)
Ear pain	1 (1.85%)	0 (0.00%)
Eye disorders		
Conjunctival haemorrhage	0 (0.00%)	1 (3.57%)
Eye irritation	0 (0.00%)	1 (3.57%)
Lacrimation increased	1 (1.85%)	0 (0.00%)
Gastrointestinal disorders		
Abdominal distension	1 (1.85%)	0 (0.00%)
Aphthous ulcer	2 (3.70%)	0 (0.00%)
Dental caries	0 (0.00%)	1 (3.57%)
Diarrhoea	2 (3.70%)	1 (3.57%)
Food poisoning	0 (0.00%)	1 (3.57%)
Glossodynia	1 (1.85%)	0 (0.00%)
Nausea	1 (1.85%)	0 (0.00%)
Toothache	1 (1.85%)	0 (0.00%)
General disorders and administration site conditions		
Cyst	1 (1.85%)	0 (0.00%)
Fatigue	2 (3.70%)	1 (3.57%)
Influenza like illness	1 (1.85%)	1 (3.57%)
Pain	0 (0.00%)	1 (3.57%)
Peripheral swelling	1 (1.85%)	0 (0.00%)
Pyrexia	1 (1.85%)	0 (0.00%)

Infections and infestations

Acarodermatitis	0 (0.00%)	1 (3.57%)
Bronchitis	0 (0.00%)	2 (7.14%)
Cellulitis	1 (1.85%)	0 (0.00%)
Conjunctivitis	2 (3.70%)	0 (0.00%)
Cystitis	1 (1.85%)	0 (0.00%)
Eye infection bacterial	0 (0.00%)	1 (3.57%)
Folliculitis	0 (0.00%)	1 (3.57%)
Gastroenteritis viral	2 (3.70%)	1 (3.57%)
Hordeolum	1 (1.85%)	0 (0.00%)
Impetigo	0 (0.00%)	1 (3.57%)
Incision site cellulitis	0 (0.00%)	1 (3.57%)
Influenza	2 (3.70%)	3 (10.71%)
Nasopharyngitis	10 (18.52%)	1 (3.57%)
Otitis externa candida	1 (1.85%)	0 (0.00%)
Otitis media	1 (1.85%)	0 (0.00%)
Pharyngitis	0 (0.00%)	1 (3.57%)
Pharyngitis streptococcal	2 (3.70%)	0 (0.00%)
Pneumonia	0 (0.00%)	1 (3.57%)
Postoperative wound infection	2 (3.70%)	1 (3.57%)
Sinusitis	1 (1.85%)	0 (0.00%)
Tinea pedis	1 (1.85%)	1 (3.57%)
Tonsillitis	1 (1.85%)	0 (0.00%)
Tooth abscess	1 (1.85%)	1 (3.57%)
Upper respiratory tract infection	7 (12.96%)	1 (3.57%)
Urinary tract infection	2 (3.70%)	2 (7.14%)

Injury, poisoning and procedural complications		
Arthropod bite	0 (0.00%)	1 (3.57%)
Fall	2 (3.70%)	0 (0.00%)
Foreign body in eye	0 (0.00%)	1 (3.57%)
Ligament rupture	1 (1.85%)	0 (0.00%)
Ligament sprain	1 (1.85%)	0 (0.00%)
Muscle strain	2 (3.70%)	0 (0.00%)
Post procedural contusion	1 (1.85%)	0 (0.00%)
Road traffic accident	1 (1.85%)	0 (0.00%)
Tendon rupture	0 (0.00%)	1 (3.57%)
Wound dehiscence	1 (1.85%)	2 (7.14%)
Investigations		
Blood pressure increased	1 (1.85%)	0 (0.00%)
Metabolism and nutrition disorders		
Decreased appetite	1 (1.85%)	0 (0.00%)
Dehydration	1 (1.85%)	0 (0.00%)
Hyperlipidaemia	0 (0.00%)	2 (7.14%)
Hypoglycaemia	1 (1.85%)	0 (0.00%)
Vitamin D deficiency	0 (0.00%)	1 (3.57%)
Musculoskeletal and connective tissue disorders		
Arthralgia	0 (0.00%)	1 (3.57%)
Back pain	4 (7.41%)	0 (0.00%)
Exostosis	0 (0.00%)	1 (3.57%)
Muscle spasms	1 (1.85%)	0 (0.00%)

Myalgia	1 (1.85%)	1 (3.57%)
Tendonitis	0 (0.00%)	1 (3.57%)
Tenosynovitis	0 (0.00%)	1 (3.57%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Basal cell carcinoma	0 (0.00%)	1 (3.57%)
Dysplastic naevus	0 (0.00%)	1 (3.57%)
Squamous cell carcinoma	1 (1.85%)	0 (0.00%)
Nervous system disorders		
Headache	3 (5.56%)	2 (7.14%)
Migraine	0 (0.00%)	1 (3.57%)
Psychiatric disorders		
Anxiety	2 (3.70%)	1 (3.57%)
Depression	0 (0.00%)	2 (7.14%)
Insomnia	1 (1.85%)	1 (3.57%)
Irritability	1 (1.85%)	0 (0.00%)
Reproductive system and breast disorders		
Testicular oedema	0 (0.00%)	1 (3.57%)
Respiratory, thoracic and mediastinal disorders		
Cough	4 (7.41%)	2 (7.14%)
Epistaxis	0 (0.00%)	1 (3.57%)
Nasal congestion	1 (1.85%)	0 (0.00%)
Oropharyngeal pain	1 (1.85%)	1 (3.57%)
Productive cough	1 (1.85%)	0 (0.00%)

Rhinorrhoea	2 (3.70%)	0 (0.00%)
Sinus congestion	2 (3.70%)	0 (0.00%)
Sneezing	1 (1.85%)	0 (0.00%)
Skin and subcutaneous tissue disorders		
Actinic keratosis	1 (1.85%)	0 (0.00%)
Dermatitis	1 (1.85%)	0 (0.00%)
Dermatitis contact	0 (0.00%)	1 (3.57%)
Hand dermatitis	0 (0.00%)	1 (3.57%)
Intertrigo	1 (1.85%)	0 (0.00%)
Pruritus	1 (1.85%)	1 (3.57%)
Pruritus generalised	1 (1.85%)	0 (0.00%)
Rash	1 (1.85%)	0 (0.00%)
Seborrhoeic dermatitis	1 (1.85%)	1 (3.57%)
Vascular disorders		
Hypertension	0 (0.00%)	3 (10.71%)

Conclusion

At Week 12, the majority of patients in the secukinumab 300 mg group showed clinical and molecular resolution of the plaques compared to placebo patients, based on clinical evaluation and immunohistochemistry findings. These findings remained consistent through Week 52.

At Week 12, 55.8% of patients in the secukinumab 300 mg group achieved PASI 90 response, compared to 0% in the placebo group. The percentage of PASI 90 response in the secukinumab group continued to be above 50% up to and including Week 52. At Week 52, 59.6% and 71.4% of patients in the secukinumab 300 mg group and placebo/secukinumab 300 mg group, respectively, were PASI 90 responders.

At Week 12, 84.6%, 78.8%, 55.8%, and 26.9% of patients achieved PASI 50, PASI 75, PASI 90, and PASI 100 responses in the secukinumab 300 mg group and 10.7%, 3.6%, 0.0%, and 0.0% achieved PASI 50, PASI 75, PASI 90, and PASI 100 responses in the placebo group. The clinical findings remained consistent up to and including Week 52, where 84.6%, 78.8%, 59.6%, and 32.7% of patients achieved PASI 50, PASI 75, PASI 90, and PASI 100 responses in the secukinumab 300 mg group, and 92.9%, 82.1%, 71.4%, and 21.4% achieved PASI 50, PASI 75, PASI 90, and PASI 100 responses in the placebo/secukinumab 300 mg group.

Biomarkers IL-19 mRNA, IL-36A mRNA, IL-37 mRNA, K16 mRNA, and beta-defensin mRNA were all analyzed from skin biopsies. Biomarkers improved in 50.0% to 79.6% ofpatients at Week 12 in the secukinumab 300 mg group compared with 10.7% to 17.9% in the placebo group. The percentages of patients with ≥ 75% improvements in specific biomarkers at Week 52 were similar between treatment groups.

The absence of K16 expression in the skin of patients treated with secukinumab 300 mg was associated with clinical responses at Week 12; among patients with PASI 90 (n = 29) and PASI 100 (n = 14) responses, K16 was not expressed in 93.1% (27/29) and 100% (14/14) of patients, respectively. At Week 52, among patients with PASI 90 (n = 47) and PASI 100 (n = 22) responses, K16 was not expressed in 57.4% (27/47) and 72.7% (16/22) of patients, respectively.

Secukinumab 300 mg treatment resulted in higher percentages of patients compared with placebo in turning off K16 expression, increasing PASI 90 responses, and improving biomarker expression. Secukinumab 300 mg confirms its known acceptable safety profile with no new signals.

Date of Clinical Trial Report

26 November 2019