Sponsor

Novartis Pharmaceuticals

Generic Drug Name

secukinumab

Trial Indication(s)

Moderate-to-severe scalp psoriasis

Protocol Number

CAIN457AUS01

Protocol Title

A randomized, double-blind, placebo-controlled, parallel-group, multicenter study to demonstrate the efficacy of subcutaneous secukinumab [300 mg] as assessed by the Psoriasis Scalp Severity Index (PSSI) at 12 weeks of treatment, compared to placebo, and to assess safety and tolerability up to 24 weeks in adult subjects with moderate to severe scalp psoriasis

Clinical Trial Phase

Phase IIIb

Phase of Drug Development

Phase IV

Study Start/End Dates

Study Start Date: 29 September 2014 (Actual first patient first visit)
Study Completion Date: 07 December 2015 (Actual last patient last visit)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This was a randomized, double-blind, placebo-controlled, parallel-group, multicenter study in 102 randomized patients with moderate-to-severe scalp psoriasis. The study consisted of 3 periods: Screening Period (up to 4 weeks), Treatment Period 1 (12 weeks), and Treatment Period 2 (12 weeks). The Screening Period was used to assess patient eligibility and to taper patients off prohibited medications and treatments. Treatment Period 1 was the period between randomization and Week 12 prior to dosing. At the start of Treatment Period 1, eligible patients were randomized in a 1:1 ratio to 1 of 2 treatment arms: secukinumab 300 mg sc or placebo sc. Visits to assess safety and efficacy were scheduled at randomization (baseline), Weeks 1, 2, 3, 4, 8, and 12 (pre-dose assessments) and then monthly for the remainder of the study. Assessments for the primary efficacy variable (PSSI 90) were performed at Week 12 (pre-dose). All patients completing Treatment Period 1 entered treatment period 2. Treatment Period 2 was the period from the Week 12 dose onwards to Week 24. During Treatment Period 2, patients in the placebo arm who achieved a PSSI 90 response (responder) at Week 12 continued to receive placebo and patients who did not achieve a PSSI 90 response (non-responder) at Week 12 were switched to secukinumab 300 mg for the remainder of the study. Patients in the secukinumab 300 mg arm continued to receive secukinumab 300 mg for the remainder of the study.

Centers

United States (17 centers)

Objectives:

The primary objective of this study was to evaluate the efficacy of secukinumab 300 mg subcutaneous (sc) compared to placebo in patients with moderate-to-severe scalp psoriasis at Week 12 with respect to the Psoriasis Scalp Severity Index (PSSI) 90 response rate.

The key secondary objective was to evaluate the efficacy of secukinumab compared to placebo in patients with moderate-to-severe scalp psoriasis at Week 12 with respect to Investigator's Global Assessment mod 2011 (IGA mod 2011) 0 or 1 response (scalp only).

Other secondary objectives of this study were:

- To evaluate the efficacy of secukinumab compared to placebo in patients with moderate-to-severe scalp psoriasis at Week 12 with respect to the change from baseline in PSSI
- To evaluate the efficacy of secukinumab compared to placebo in patients with moderate-to-severe scalp psoriasis at Week 12 with respect to PSSI 75 response rate
- To evaluate the efficacy of secukinumab compared to placebo in patients with moderate-to-severe scalp psoriasis at Week 12 with respect to PSSI 100 response rate
- To evaluate the speed of onset of the clinical effect of secukinumab compared to placebo in patients with moderate-to-severe scalp psoriasis based on time to 50% reduction in PSSI
- To evaluate the efficacy of secukinumab compared to placebo in patients with moderate-to-severe scalp psoriasis at Week 12 with respect to Psoriasis Area and Severity Index (PASI) 75, PASI 90, and PASI 100 response rates
- To evaluate the efficacy of secukinumab compared to placebo in patients with moderate-to-severe scalp psoriasis at Week 12 with respect to IGA mod 2011 0 or 1 response (entire body including scalp)
- To evaluate the effects of secukinumab compared to placebo in patients with moderate-to-severe scalp psoriasis at Week 12 with respect to changes from baseline in the Subject Assessment of Pain, Itching and Scaling (11-point scale [0-10]) (scalp only)
- To evaluate the clinical safety and tolerability of secukinumab as assessed by vital signs, clinical laboratory variables, electrocardiogram (ECG), and adverse events (AEs) monitoring

Test Product (s), Dose(s), and Mode(s) of Administration

Dosage form:
Secukinumab 150 mg (1 mL liquid formulation) in pre-filled syringes and placebo pre-filled syringes (1 mL liquid formulation)

Mode of administration:
Subcutaneous injection

Dosage:
Each secukinumab 300 mg dose was given as 2 sc injections of secukinumab 150 mg.
Each placebo to secukinumab 300 mg dose was given as two 150 mg sc injections, each containing a mixture of inactive excipients, matching the composition of the secukinumab 150 mg dose.

Statistical Methods

Statistical analyses of efficacy variables were performed on an intent-to-treat basis, involving all randomized patients who were assigned to study treatment (Full analysis set, FAS). Baseline characteristics were analyzed for all randomized patients. Safety analyses were performed for all randomized patients who received at least 1 dose of study treatment (Safety set).

Efficacy and safety data for Treatment Period 1 (up to Week 12 pre-dose) are summarized by the randomized treatment groups (secukinumab 300 mg and placebo), efficacy data for Treatment Period 2 (Week 12 post-dose to Week 24) are summarized for secukinumab 300 mg and placebo-secukinumab 300 mg groups, and safety data for the entire treatment period up to Week 24 are summarized by all treatment groups (secukinumab 300 mg, placebo-secukinumab 300 mg, Any secukinumab, and placebo). The Any secukinumab group includes all patients who received ≥ 1 dose of secukinumab.

The primary efficacy variable (PSSI 90) was analyzed using the Cochran-Mantel-Haenszel test to compare secukinumab and placebo, adjusting for body weight (<90 kg, ≥90 kg). A 95% confidence interval for the difference between the 2 treatment groups in the proportion of patients who were PSSI 90 responders was calculated using the normal approximation to the binomial distribution. The primary analysis of the primary efficacy variable was based on the FAS. Analysis of the key secondary efficacy variable (IGA mod 2011 0/1 scalp only) used the same approach as for the primary efficacy variable.

A hierarchical hypothesis testing approach was employed for the primary and key secondary efficacy variables at Week 12. If a statistically significant difference between the 2 treatment groups was obtained for PSSI 90 (ie, p-value ≤0.05), hypothesis testing to compare the 2 treatment groups with respect to the IGA mod 2011 0/1 scalp only was performed at the 0.05 significance level.

Supportive analyses of PSSI 90 and IGA mod 2011 0/1 (scalp only) response at Week 12 were performed using logistic regression with treatment, body weight (<90 kg, ≥90 kg), previous systemic therapy (yes, no), previous biologic therapy (yes, no), and previous tumor necrosis factor (TNF)α-inhibitor therapy (yes, no) as explanatory variables. The odds ratios for secukinumab versus placebo, 95% confidence interval for the odds ratios, and p-value based on the fitted model were reported. A sensitivity analysis was also performed for these variables using multiple imputation for missing data.

The assessment of safety was based mainly on the frequency of AEs, laboratory data, vital signs, ECGs and immunogenicity. AEs and AESIs were summarized for Treatment Period 1 (absolute incidence) and the entire treatment period (absolute incidence and exposure-adjusted incidence rate per 100 patient-years). Separate summaries were provided for deaths, SAEs, other significant AEs leading to discontinuation and AEs leading to dose interruption. The summary of laboratory evaluations was presented for hematology and clinical chemistry analyzed with respect to Common Terminology Criteria for Adverse Events (CTCAE) grades, shifts in CTCAE grades, change from baseline and maximum change from baseline. Any events of lipase >3×ULN and/or amylase >3×ULN, or notably abnormal liver-related events were also summarized. In addition, changes from baseline in vital signs and ECGs data were summarized by treatment group.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
- Chronic scalp psoriasis for at least the previous six months
- Moderate to severe scalp psoriasis as defined by a PSSI score of ≥12 and 30% or higher of scalp surface area affected
- Must be candidates for systemic therapy, which means having scalp psoriasis inadequately controlled by topical treatments (corticosteroids), and/or phototherapy, and/or previous systemic therapy.

Exclusion Criteria:
- Forms of psoriasis other than chronic plaque
- Drug-induced psoriasis (e.g., new onset or current exacerbation from β-blockers, calcium channel inhibitors)
- Ongoing use of prohibited treatments (e.g., topical or systemic corticosteroids, UV therapy)
- Prior exposure to secukinumab (AIN457) or any other biologic drug directly targeting IL17A or IL-17RA receptors
- Use of other investigational drugs within 30 days prior to study entry, or within a period of 5 half-lives of the investigational treatment, whichever is longer
- Active, ongoing inflammatory diseases other than psoriasis that might confound the evaluation of the benefit of secukinumab
- Active system infections (with the exception of the common cold) during the two weeks prior to starting study treatment
- Other protocol-defined inclusion/exclusion criteria may apply

Participant Flow Table

Period 1 (Randomized Set)

	Secukinumab	Placebo
Started	51	51
Completed	50	47
Not Completed	1	4
Withdrawal by Subject	1	3
Lost to Follow-up	0	1

Period 2 (Randomized Set)

	Secukinumab	Placebo
Started	50	47
Completed	46	46
Not Completed	4	1
Lost to Follow-up	1	1
Adverse Event	2	0
Withdrawal by Subject	1	0

Baseline Characteristics

	Secukinumab	Placebo	Total
Number of Participants [units: participants]	51	51	102
Age, Customized (units: Age (years)) Mean ± Standard Deviation	42.7±13.39	41.1±14.17	41.9±13.74
Gender, Male/Female (units: participants)			
Female	24	30	54
Male	27	21	48

Summary of Efficacy

Primary Outcome Result(s)

Psoriasis Scalp Severity Index 90 (PSSI 90)

	Secukinumab	Placebo
Number of Participants Analyzed [units: participants]	51	51
Psoriasis Scalp Severity Index 90 (PSSI 90) (units: Percent of Participants)	52.9	2.0

Statistical Analysis

Groups	Secukinumab, Placebo	
Non-Inferiority/Equivalence Test	No	
P Value	<0.001	
Method	Cochran-Mantel-Haenszel	adjusted for body weight (< 90 kg, ≥ 90 kg)
95% Confidence Interval 2-Sided	37 to 65	

Secondary Outcome Result(s)

Secondary: Investigator's Global Assessment model 2011 (IGA mod 2011) score of 0 or 1 (scalp only)

	Secukinumab	Placebo
Number of Participants Analyzed [units: participants]	51	51
Secondary: Investigator's Global Assessment model 2011 (IGA mod 2011) score of 0 or 1 (scalp only) (units: % of Participants)	56.9	5.9

Change from baseline in PSSI score

	Secukinumab	Placebo
Number of Participants Analyzed [units: participants]	51	51
Change from baseline in PSSI score (units: Score) Mean ± Standard Deviation	-25.47 ± 17.052	-5.98 ± 12.868

Psoriasis Scalp Severity Index 75 (PSSI 75) response

	Secukinumab	Placebo

Number of Participants Analyzed [units: participants]	51	51
Psoriasis Scalp Severity Index 75 (PSSI 75) response (units: % of Participants)	62.7	5.9

Psoriasis Scalp Severity Index 100 (PSSI 100) response

	Secukinumab	Placebo
Number of Participants Analyzed [units: participants]	51	51
Psoriasis Scalp Severity Index 100 (PSSI 100) response (units: % of Participants)	35.3	0.0

Time to 50% reduction in Psoriasis Scalp Severity Index (PSSI) score

	Secukinumab	Placebo
Number of Participants Analyzed [units: participants]	51	51
Time to 50% reduction in Psoriasis Scalp Severity Index (PSSI) score (units: % of Participants)	78.0	31.4

Psoriasis Area and Severity Index 75 (PASI 75)

	Secukinumab	Placebo
Number of Participants Analyzed [units: participants]	51	51
Psoriasis Area and Severity Index 75 (PASI 75) (units: % of participants)	64.7	2.0

Psoriasis Area and Severity Index 90 (PASI 90)

	Secukinumab	Placebo
Number of Participants Analyzed [units: participants]	51	51
Psoriasis Area and Severity Index 90 (PASI 90) (units: % of Participants)	47.1	0.0

Psoriasis Area and Severity Index 100 (PASI 100)

	Secukinumab	Placebo
Number of Participants Analyzed [units: participants]	51	51
Psoriasis Area and Severity Index 100 (PASI 100) (units: % of Participants)	23.5	0.0

Investigator's Global Assessment model 2011 (GA mod 2011) score of 0 or 1 (entire body including scalp)

	Secukinumab	Placebo
Number of Participants Analyzed [units: participants]	51	51
Investigator's Global Assessment model 2011 (GA mod 2011) score of 0 or 1 (entire body including scalp) (units: % of Participants)	52.9	3.9

Change from baseline in Subject Assessment of Pain

	Secukinumab	Placebo
Number of Participants Analyzed [units: participants]	51	51
Change from baseline in Subject Assessment of Pain (units: Score) Mean ± Standard Deviation	-1.43 ± 3.233	1.04 ± 2.615

Change from baseline in Subject Assessment of Itching

	Secukinumab	Placebo
Number of Participants Analyzed [units: participants]	51	51

Change from baseline in Subject Assessment of Itching (units: Score) Mean ± Standard Deviation	-4.10 ± 3.008	-0.24 ± 2.840

Change from baseline in Subject Assessment of Scaling (scalp only)

	Secukinumab	Placebo
Number of Participants Analyzed [units: participants]	51	51
Change from baseline in Subject Assessment of Scaling (scalp only) (units: Participants) Mean ± Standard Deviation	-5.24 ± 2.861	-0.65 ± 2.763

Summary of Safety

Safety Results

Serious Adverse Events by System Organ Class

Time Frame	Timeframe for AE
Additional Description	AE additional description
Source Vocabulary for Table Default	MedDRA (18.1)
Assessment Type for Table Default	Systematic Assessment

	Treatment Period 1 Secukinumab 300 mg N = 51	Treatment Period 1 Placebo N = 51	Treatment Period 2 Placebo/Secukinumab 300 mg N = 46	Treatment Period 2: Any Secukinumab N = 96
Total participants affected	0 (0.00%)	1 (1.96%)	1 (2.17%)	1 (1.04%)
INFECTIONS AND INFESTATIONS				
CELLULITIS	0 (0.00%)	1 (1.96%)	1 (2.17%)	1 (1.04%)

Other Adverse Events by System Organ Class

Time Frame	Timeframe for AE
Additional Description	AE additional description
Source Vocabulary for Table Default	MedDRA (18.1)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	Treatment Period 1 Secukinumab 300 mg N = 51	Treatment Period 1 Placebo N = 51	Treatment Period 2 Placebo/Secukinumab 300 mg N = 46	Treatment Period 2: Any Secukinumab N = 96
Total participants affected	8 (15.69%)	5 (9.80%)	5 (10.87%)	5 (5.21%)
GASTROINTESTINAL DISORDERS				

DIARRHOEA	2 (3.92%)	2 (3.92%)	3 (6.52%)	3 (3.13%)
INFECTIONS AND INFESTATIONS				
NASOPHARYNGITIS	3 (5.88%)	1 (1.96%)	1 (2.17%)	1 (1.04%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS				
DERMATITIS CONTACT	3 (5.88%)	2 (3.92%)	1 (2.17%)	1 (1.04%)

Conclusion:

Secukinumab 300 mg was superior to placebo in the treatment of patients with moderate-to-severe scalp psoriasis. Secukinumab 300 mg provided a rapid onset of response and was significantly better than placebo in achieving almost clear to clear resolution of scalp psoriasis (PSSI 90 and IGA mod 2011 0/1 scalp only) at Week 12. The greater efficacy of secukinumab 300 mg vs. placebo extended across all variables in scalp psoriasis (PSSI 75/90/100 and IGA mod 2011 0/1 scalp only) and full body psoriasis (PASI 75/90/100 and IGA mod 2011 0/1 full body) at Week 12, indicating higher levels of scalp and skin clearance with secukinumab. Secukinumab 300 mg also showed greater improvements in scalp pain, itching and scaling and scalp-specific quality of life. All efficacy responses were sustained or further improved through Week 24. The safety profile of secukinumab 300 mg in this study showed no new or unexpected signals and was fully consistent with the known safety profile for secukinumab.

Date of Clinical Trial Report

07 December 2016