NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Secukinumab (AIN457)

Trial Indication(s)

Moderate to severe chronic plaque-type psoriasis

Protocol Number

CAIN457A2324

Protocol Title

A randomized, double-blind, multicenter study assessing short and long-term efficacy, safety, and tolerability of sub-cutaneous secukinumab in subjects of body weight 90 kg or higher with moderate to severe chronic plaque-type psoriasis

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase IIIB

Study Start/End Dates

Study Start Date: June 2018 (Actual)
Primary Completion Date: September 2019 (Actual)
Study Completion Date: July 2020 (Actual)

Reason for Termination (If applicable)

Study Design/Methodology

This was a 52-week multicenter, randomized, double-blind, parallel-group trial, planned to be conducted in approximately 330 patients with moderate to severe chronic plaque-type psoriasis of body weight 90 kg or higher at time of randomization. The study consisted of 4 periods: Screening (up to 4 weeks), Treatment Period 1 (16 weeks), Treatment Period 2 (36 weeks), and Follow-up (8 weeks).

At the start of Treatment Period 1, eligible patients were randomized to one of the following treatment groups in approximately 1:1 ratio: secukinumab 300 mg Q2W (every 2 weeks) and secukinumab 300 mg Q4W (every 4 weeks). All patients received two injections of secukinumab 150 mg once weekly for the first four weeks (at randomization, Weeks 1, 2 and 3). Thereafter the frequency of secukinumab/placebo injections was per the treatment groups assigned at baseline. To maintain the treatment blind, patients assigned to receive secukinumab 300 mg Q4W also received two placebo injections (2 x secukinumab placebo 150 mg s.c) every 4 weeks starting at Week 6.

Subjects who completed Treatment Period 1 entered Treatment Period 2. Patients had been randomized at baseline visit in a 2:1:1 ratio into one of the treatment groups:

Secukinumab 300mg Q2W: patients remained on secukinumab 300 mg Q2W until the end of Treatment

Secukinumab 300mg Q4W: patients continued on 300 mg Q4W during Treatment Period 2 regardless of their PASI 90 response status at Week 16

Secukinumab 300mg Q4W possible up-titration: patients received secukinumab 300 mg Q4W up to Week 16, and then based on their Psoriasis Area and Severity Index (PASI) 90 response status at Week 16:

- PASI 90 responders: remained on secukinumab 300 mg Q4W during Treatment Period 2

- PASI 90 non-responders: were up-titrated to secukinumab 300 mg Q2W during Treatment Period 2

All patients entered the post treatment follow-up period, which included the F4 and F8 follow-up visits. Follow-up visit F4 was approximately 4 weeks after the End of Treatment Period 1 (EOT 1) / End of Treatment Period 2 (EOT 2) visit and 8 weeks after the last study treatment administration. Follow-up visit F8 was approximately 8 weeks after the EOT1/EOT2 visit, and 12 weeks after the last study treatment administration.

Centers

67 centers in 7 countries: Germany(6), United States(38), Canada(6), Italy(5), Russia(7), Czech Republic(2), Hungary(3)

Objectives:

Primary objective:

To demonstrate the efficacy of secukinumab 300 mg every 2 weeks in comparison to secukinumab 300 mg every 4 weeks with respect to Psoriasis Area and Severity Index (PASI) 90 response at Week 16.

Secondary objectives:

To demonstrate the efficacy of secukinumab 300 mg every 2 weeks in comparison to secukinumab 300 mg every 4 weeks with respect to Investigator's Global Assessment modified (IGA mod) 2011 0 or 1 response at Week 16.

To investigate the clinical safety and tolerability of secukinumab 300 mg every 2 weeks as assessed by vital signs, clinical laboratory variables, electrocardiogram (ECG) and adverse events (AEs) monitoring in comparison to secukinumab 300 mg every 4 weeks.

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

Secukinumab 150 mg solution for subcutaneous (sc) injection in a 1 mL prefilled syringe (PFS)

Placebo solution for sc injection in a 1 mL PFS matching the composition and appearance of secukinumab 150 mg dose

Statistical Methods

The analysis of efficacy variables was based on the full analysis set (FAS). The primary variable in the testing strategy was PASI 90 response at Week 16 (for superiority comparison of secukinumab 300 mg Q2W versus secukinumab 300 mg Q4W). The secondary efficacy variable in the testing strategy was IGA mod 2011 0 or 1 response at Week 16 (for superiority comparison of secukinumab 300 mg Q2W versus secukinumab 300 mg Q4W), which was analyzed analogously to the primary analysis.

All safety evaluations were performed on the Safety set.

Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria:
-Written informed consent must have been obtained before any assessment was performed. Where relevant, a legal representative will also have signed the informed study consent according to local laws and regulations.
-Subjects must have been able to understand and communicate with the investigator and comply with the requirements of the study.
-Men or women at least 18 years of age at time of screening.
-Body weight of ≥ 90 kg at the time of randomization.
-Chronic plaque-type psoriasis present for at least 6 months and diagnosed before randomization.
-Moderate to severe psoriasis as defined at randomization by:
• Psoriasis Area and Severity Index (PASI) score of 12 or greater, and
• Investigator's Global Assessment (IGA) mod 2011 score of 3 or greater (based on a static scale of 0 – 4), and
• Body Surface Area (BSA) affected by plaque-type psoriasis of 10% or greater.
-Candidate for systemic therapy. This is defined as a subject having moderate to severe chronic plaque-type psoriasis that is inadequately controlled by:
• topical treatment and/or,
• phototherapy and/or,
• previous systemic therapy.

Key Exclusion Criteria:
-Forms of psoriasis other than chronic plaque-type (e.g., pustular, erythrodermic and guttate psoriasis) at screening or Randomization.
-Ongoing use of prohibited treatments. Washout periods detailed in the protocol have to be adhered to. Subjects not willing to limit

ultraviolet (UV) light exposure (e.g., sunbathing and / or the use of tanning devices) during the course of the study will be considered not eligible for this study since UV light exposure is prohibited. Note: administration of live vaccines 6 weeks prior to Randomization or during the study period is also prohibited.
-Previous exposure to secukinumab (AIN457) or any other biologic drug directly targeting Interleukin-17 (IL-17) or the IL-17 receptor.
-Use of other investigational drugs at the time of enrollment, or within 5 half-lives of enrollment, or within 4 weeks until the expected pharmacodynamic effect has returned to baseline, whichever is longer; or longer if required by local regulations.
-Pregnant or nursing (lactating) women
-History of lymphoproliferative disease or any known malignancy or history of malignancy of any organ system treated or untreated within the past 5 years, regardless of whether there is evidence of local recurrence or metastases (except for skin Bowen's disease, or basal cell carcinoma or actinic keratoses that have been treated with no evidence of recurrence in the past 12 weeks; carcinoma in situ of the cervix or non-invasive malignant colon polyps that have been removed).
-History of hypersensitivity to any of the study drug constituents.

Participant Flow Table

Overall Study

	Secukinumab 300 mg every 2 weeks (Q2W)	Secukinumab 300 mg every 4 weeks (Q4W) (safety)	Secukinumab 300 mg every 4 weeks non-responders up-titration (Q4W NR up)	Total
Arm/Group Description	2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until	2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter Q4W. Includes both subjects randomized to remain on Q4W the entire treatment period, and	2 injections of secukinumab 150 mg once weekly up to week 4, then Q4W up to Week 16 and thereafter Q2W. Includes Psoriasis Area and Severity Index (PASI) 90 non-responders	

	the end of treatment.	subjects that were Psoriasis Area and Severity Index (PASI) 90 responders at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group.	(NR) at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group (subjects randomized to switch to Q2W if PASI 90 non-responder at Week 16).	
Started	165	135	31	331
Completed	148	117	28	293
Not Completed	17	18	3	38
Withdrawal of informed consent	2	1	0	3
Withdrawal by Subject	5	5	1	11
Lost to Follow-up	4	1	0	5
New therapy for study indication	1	0	0	1
Lack of Efficacy	1	2	0	3
Death	0	1	0	1
Adverse Event	4	8	2	14

Baseline Characteristics

	Secukinumab 300 mg every 2 weeks (Q2W)	Secukinumab 300 mg every 4 weeks (Q4W) (safety)	Secukinumab 300 mg every 4 weeks non-responders up-titration (Q4W NR up)	Total
Arm/Group Description	2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until the end of treatment.	2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter Q4W. Includes both subjects randomized to remain on Q4W the entire treatment period, and subjects that were Psoriasis Area and Severity Index (PASI) 90 responders at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group.	2 injections of secukinumab 150 mg once weekly up to week 4, then Q4W up to Week 16 and thereafter Q2W. Includes Psoriasis Area and Severity Index (PASI) 90 non-responders (NR) at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group (subjects randomized to switch to Q2W if PASI 90 non-responder at Week 16).	
Number of Participants [units: participants]	165	135	31	331

Age Continuous (units: years) Mean ± Standard Deviation				
	48.2±12.73	46.1±13.24	44.7±13.61	47.1±13.04
Sex: Female, Male (units: participants) Count of Participants (Not Applicable)				
Female	39	34	10	83
Male	126	101	21	248
Race (NIH/OMB) (units: participants) Count of Participants (Not Applicable)				
American Indian or Alaska Native	1	1	0	2
Asian	4	4	1	9
Native Hawaiian or Other Pacific Islander	2	0	0	2
Black or African American	7	5	0	12
White	151	125	30	306
More than one race	0	0	0	0
Unknown or Not Reported	0	0	0	0

Primary Outcome Result(s)

Percentage of subjects who achieve 90% or greater reduction in Psoriasis Area and Severity Index (PASI) score – week 16 (Full analysis set)

(Time Frame: 16 weeks)

	Secukinumab 300 mg every 2 weeks (Q2W)	Secukinumab 300 mg every 4 weeks (Q4W) (up to week 16 pre-dose)
Arm/Group Description	2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until the end of treatment.	Subjects received 2 injections of secukinumab 150 mg once weekly for four weeks (at Randomization, Weeks 1, 2 and 3), followed by 2 injections of secukinumab 150 mg every four weeks, starting at Week 4 and up to Week 12.
Number of Participants Analyzed [units: participants]	165	166
Percentage of subjects who achieve 90% or greater reduction in Psoriasis Area and Severity Index (PASI) score – week 16 (Full analysis set) (units: Participants) Count of Participants (Not Applicable)		

rounded average number of patients with response in 100 imputations at week 16 for PASI 90	121 (73.33%)	92 (55.42%)

Statistical Analysis

Groups	Secukinumab 300 mg every 2 weeks (Q2W), Secukinumab 300 mg every 4 weeks (Q4W) (up to week 16 pre-dose)	
P Value	0.0003	One-sided p-value
Method	Regression, Logistic	
Risk Difference (RD)	17.72	
95 % Confidence Interval 2-Sided	7.45 to 27.98	

Statistical Analysis

Groups	Secukinumab 300 mg every 2 weeks (Q2W), Secukinumab 300 mg every 4 weeks (Q4W) (up to week 16 pre-dose)	
P Value	0.0003	One-sided p-value
Method	Regression, Logistic	
Odds Ratio (OR)	2.33	

95 % Confidence Interval 2-Sided	1.44 to 3.78

Secondary Outcome Result(s)

Percentage of subjects who achieve Investigator Global Assessment (IGA modified 2011) score of 0 or 1 - week 16 (Full analysis set)

(Time Frame: 16 weeks)

	Secukinumab 300 mg every 2 weeks (Q2W)	Secukinumab 300 mg every 4 weeks (Q4W) (up to week 16 pre-dose)
Arm/Group Description	2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until the end of treatment.	Subjects received 2 injections of secukinumab 150 mg once weekly for four weeks (at Randomization, Weeks 1, 2 and 3), followed by 2 injections of secukinumab 150 mg every four weeks, starting at Week 4 and up to Week 12.
Number of Participants Analyzed [units: participants]	165	166
Percentage of subjects who achieve Investigator		

Global Assessment (IGA modified 2011) score of 0 or 1 - week 16 (Full analysis set) (units: Participants) Count of Participants (Not Applicable)		
rounded average number of patients with response in 100 imputations at week 16 for IGA 0/1	122 (73.94%)	109 (65.66%)

Statistical Analysis

Groups	Secukinumab 300 mg every 2 weeks (Q2W), Secukinumab 300 mg every 4 weeks (Q4W) (up to week 16 pre-dose)	
P Value	0.0498	One-sided p-value
Method	Regression, Logistic	
Risk Difference (RD)	8.28	
95 % Confidence Interval 2-Sided	-1.65 to 18.20	

Statistical Analysis

Groups	Secukinumab 300 mg every 2 weeks (Q2W), Secukinumab 300 mg every 4 weeks (Q4W) (up to week 16 pre-dose)	
P Value	0.0498	One-sided p-value

Method	Regression, Logistic
Odds Ratio (OR)	1.51
95 % Confidence Interval 2-Sided	0.92 to 2.47

Absolute and relative frequencies for deaths, other serious or clinically significant adverse events or related discontinuations - Entire Study Period (Safety set)

(Time Frame: Adverse events were reported from first dose of study treatment until end of study treatment plus 8 weeks post treatment, up to a maximum timeframe of 470 days.)

	Secukinumab 300 mg every 2 weeks (Q2W)	Secukinumab 300 mg every 4 weeks (Q4W) (safety)	Secukinumab 300 mg every 4 weeks non-responders up-titration (Q4W NR up)
Arm/Group Description	2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until the end of treatment.	2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter Q4W. Includes both subjects randomized to remain on Q4W the entire treatment period, and subjects that were Psoriasis Area and Severity Index (PASI) 90 responders at	2 injections of secukinumab 150 mg once weekly up to week 4, then Q4W up to Week 16 and thereafter Q2W. Includes Psoriasis Area and Severity Index (PASI) 90 non-responders (NR) at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group

		Week 16 from the secukinumab 300 mg Q4W possible up-titrate group.	(subjects randomized to switch to Q2W if PASI 90 non-responder at Week 16).
Number of Participants Analyzed [units: participants]	165	134	31
Absolute and relative frequencies for deaths, other serious or clinically significant adverse events or related discontinuations - Entire Study Period (Safety set) (units: Participants) Count of Participants (Not Applicable)			
Patients with any AE(s)	127 (76.97%)	97 (72.39%)	24 (77.42%)
Patients with serious or other significant events - Death	0 (%)	1 (.75%)	0 (%)
Patients with serious or other significant events - Non-fatal SAE(s)	14 (8.48%)	17 (12.69%)	4 (12.9%)
Patients with serious or other significant events - Discontinued study treatment due to any AE(s)	4 (2.42%)	9 (6.72%)	2 (6.45%)

Safety Results

All-Cause Mortality

	Secukinumab 300 mg every 2 weeks (Q2W) N = 165	Secukinumab 300 mg every 4 weeks (Q4W) (safety) N = 134	Secukinumab 300 mg every 4 weeks non-responders up-titration (Q4W NR up) N = 31	All Patients N = 330
Arm/Group Description	2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until the end of treatment.	2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter Q4W. Includes both subjects randomized to remain on Q4W the entire treatment period, and subjects that were Psoriasis Area and Severity Index (PASI) 90 responders at Week 16 from the secukinumab	2 injections of secukinumab 150 mg once weekly up to week 4, then Q4W up to Week 16 and thereafter Q2W. Includes Psoriasis Area and Severity Index (PASI) 90 non-responders (NR) at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group (subjects randomized to switch to Q2W	All Patients

		300 mg Q4W possible up-titrate group.	if PASI 90 non-responder at Week 16).	
Total participants affected	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)

Serious Adverse Events by System Organ Class

Time Frame	Adverse events were reported from first dose of study treatment until end of study treatment plus 8 weeks post treatment, up to a maximum timeframe of 470 days.
Source Vocabulary for Table Default	MedDRA (23.0)
Assessment Type for Table Default	Systematic Assessment

	Secukinumab 300 mg every 2 weeks (Q2W) N = 165	**Secukinumab 300 mg every 4 weeks (Q4W) (safety) N = 134**	**Secukinumab 300 mg every 4 weeks non-responders up-titration (Q4W NR up) N = 31**	**All Patients N = 330**
Arm/Group Description	2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until	2 injections of secukinumab 150 mg once weekly up to week 4 and thereafter Q4W. Includes both subjects randomized to remain on Q4W the entire	2 injections of secukinumab 150 mg once weekly up to week 4, then Q4W up to Week 16 and thereafter Q2W. Includes Psoriasis Area and Severity Index (PASI)	All Patients

	the end of treatment.	treatment period, and subjects that were Psoriasis Area and Severity Index (PASI) 90 responders at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group.	90 non-responders (NR) at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group (subjects randomized to switch to Q2W if PASI 90 non-responder at Week 16).	
Total participants affected	14 (8.48%)	18 (13.43%)	4 (12.90%)	36 (10.91%)
Cardiac disorders				
Acute myocardial infarction	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Atrial fibrillation	0 (0.00%)	1 (0.75%)	1 (3.23%)	2 (0.61%)
Cardiac arrest	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Diastolic dysfunction	1 (0.61%)	0 (0.00%)	0 (0.00%)	1 (0.30%)
Tachycardia	0 (0.00%)	1 (0.75%)	1 (3.23%)	2 (0.61%)
Ear and labyrinth disorders				
Deafness	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Tinnitus	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Gastrointestinal disorders				
Diverticulum intestinal haemorrhagic	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Dysphagia	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)

Inguinal hernia	0 (0.00%)	0 (0.00%)	1 (3.23%)	1 (0.30%)
Retroperitoneal mass	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Umbilical hernia, obstructive	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
General disorders and administration site conditions				
Asthenia	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Non-cardiac chest pain	2 (1.21%)	0 (0.00%)	0 (0.00%)	2 (0.61%)
Hepatobiliary disorders				
Cholecystitis chronic	0 (0.00%)	0 (0.00%)	1 (3.23%)	1 (0.30%)
Cholestatic liver injury	1 (0.61%)	0 (0.00%)	0 (0.00%)	1 (0.30%)
Infections and infestations				
Acute HIV infection	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Breast cellulitis	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Clostridium difficile infection	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Endocarditis bacterial	1 (0.61%)	0 (0.00%)	0 (0.00%)	1 (0.30%)
Erysipelas	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Pneumonia	0 (0.00%)	0 (0.00%)	1 (3.23%)	1 (0.30%)
Sepsis	0 (0.00%)	2 (1.49%)	0 (0.00%)	2 (0.61%)
Subcutaneous abscess	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Tooth abscess	0 (0.00%)	0 (0.00%)	1 (3.23%)	1 (0.30%)
Injury, poisoning and procedural complications				
Blast injury	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)

Fall	1 (0.61%)	0 (0.00%)	1 (3.23%)	2 (0.61%)
Joint injury	1 (0.61%)	0 (0.00%)	0 (0.00%)	1 (0.30%)
Ligament rupture	1 (0.61%)	0 (0.00%)	0 (0.00%)	1 (0.30%)
Multiple injuries	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Periprosthetic fracture	1 (0.61%)	0 (0.00%)	0 (0.00%)	1 (0.30%)
Procedural pain	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Road traffic accident	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Investigations				
Gamma-glutamyltransferase increased	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Lipase increased	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Metabolism and nutrition disorders				
Dehydration	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Diabetic ketoacidosis	1 (0.61%)	0 (0.00%)	0 (0.00%)	1 (0.30%)
Musculoskeletal and connective tissue disorders				
Cervical spinal stenosis	1 (0.61%)	0 (0.00%)	0 (0.00%)	1 (0.30%)
Fibromyalgia	1 (0.61%)	0 (0.00%)	0 (0.00%)	1 (0.30%)
Rotator cuff syndrome	1 (0.61%)	0 (0.00%)	0 (0.00%)	1 (0.30%)
Nervous system disorders				
Quadriplegia	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)
Psychiatric disorders				
Depression	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)

Respiratory, thoracic and mediastinal disorders				
Dyspnoea	1 (0.61%)	1 (0.75%)	0 (0.00%)	2 (0.61%)
Epistaxis	1 (0.61%)	0 (0.00%)	0 (0.00%)	1 (0.30%)
Sleep apnoea syndrome	1 (0.61%)	0 (0.00%)	0 (0.00%)	1 (0.30%)
Vascular disorders				
Peripheral ischaemia	0 (0.00%)	1 (0.75%)	0 (0.00%)	1 (0.30%)

Other Adverse Events by System Organ Class

Time Frame	Adverse events were reported from first dose of study treatment until end of study treatment plus 8 weeks post treatment, up to a maximum timeframe of 470 days.
Source Vocabulary for Table Default	MedDRA (23.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	Secukinumab 300 mg every 2 weeks (Q2W) N = 165	**Secukinumab 300 mg every 4 weeks (Q4W) (safety) N = 134**	**Secukinumab 300 mg every 4 weeks non-responders up-titration (Q4W NR up) N = 31**	**All Patients N = 330**
Arm/Group Description	2 injections of secukinumab 150 mg once weekly up to week 4 and	2 injections of secukinumab 150 mg once weekly up to week 4 and	2 injections of secukinumab 150 mg once weekly up to week 4, then	All Patients

	thereafter every 2 weeks. Subjects remained on secukinumab 300 mg every 2 weeks until the end of treatment.	thereafter Q4W. Includes both subjects randomized to remain on Q4W the entire treatment period, and subjects that were Psoriasis Area and Severity Index (PASI) 90 responders at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group.	Q4W up to Week 16 and thereafter Q2W. Includes Psoriasis Area and Severity Index (PASI) 90 non-responders (NR) at Week 16 from the secukinumab 300 mg Q4W possible up-titrate group (subjects randomized to switch to Q2W if PASI 90 non-responder at Week 16).	
Total participants affected	66 (40.00%)	57 (42.54%)	16 (51.61%)	139 (42.12%)
Gastrointestinal disorders				
Diarrhoea	10 (6.06%)	6 (4.48%)	2 (6.45%)	18 (5.45%)
Nausea	1 (0.61%)	4 (2.99%)	2 (6.45%)	7 (2.12%)
General disorders and administration site conditions				
Fatigue	4 (2.42%)	3 (2.24%)	2 (6.45%)	9 (2.73%)
Pyrexia	2 (1.21%)	2 (1.49%)	2 (6.45%)	6 (1.82%)
Infections and infestations				
Nasopharyngitis	32 (19.39%)	22 (16.42%)	5 (16.13%)	59 (17.88%)

Tooth abscess	1 (0.61%)	0 (0.00%)	2 (6.45%)	3 (0.91%)
Upper respiratory tract infection	12 (7.27%)	9 (6.72%)	3 (9.68%)	24 (7.27%)
Urinary tract infection	1 (0.61%)	5 (3.73%)	2 (6.45%)	8 (2.42%)
Injury, poisoning and procedural complications				
Arthropod bite	0 (0.00%)	1 (0.75%)	2 (6.45%)	3 (0.91%)
Investigations				
Neutrophil count decreased	1 (0.61%)	3 (2.24%)	3 (9.68%)	7 (2.12%)
Metabolism and nutrition disorders				
Diabetes mellitus	3 (1.82%)	0 (0.00%)	2 (6.45%)	5 (1.52%)
Musculoskeletal and connective tissue disorders				
Arthralgia	7 (4.24%)	6 (4.48%)	2 (6.45%)	15 (4.55%)
Back pain	3 (1.82%)	6 (4.48%)	2 (6.45%)	11 (3.33%)
Nervous system disorders				
Headache	11 (6.67%)	6 (4.48%)	1 (3.23%)	18 (5.45%)
Respiratory, thoracic and mediastinal disorders				
Cough	7 (4.24%)	2 (1.49%)	2 (6.45%)	11 (3.33%)
Oropharyngeal pain	3 (1.82%)	7 (5.22%)	2 (6.45%)	12 (3.64%)
Skin and subcutaneous tissue disorders				

Intertrigo	4 (2.42%)	0 (0.00%)	3 (9.68%)	7 (2.12%)

Conclusion:

The Week 16 analysis demonstrated that the secukinumab 300 mg Q2W dose regimen was superior to the secukinumab 300 mg Q4W dose regimen in the treatment of moderate to severe chronic plaque-type psoriasis in heavier patients (>= 90 kg) with respect to the primary endpoint of PASI 90 response at Week 16. The secukinumab 300 mg Q2W dose regimen also showed numerically greater efficacy in the secondary endpoint of IGA mod 2011 0/1 response at Week 16.

Secukinumab was well tolerated at both dose regimens (Q2W and Q4W). The safety was comparable between the secukinumab 300 mg Q2W and secukinumab 300 mg Q4W groups. There were no dose-dependent increases in the incidence of AEs or risks. The safety profile in this study was consistent with the known safety profile of secukinumab and showed no new or unexpected safety signals.

Date of Clinical Trial Report

27 Jan 2021