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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Secukinumab

Trial Indication

hidradenitis suppurativa (HS)

Protocol Number

CAIN457M2301

Protocol Title

A randomized, double-blind, multi-center study assessing short (16 weeks) and long-term efficacy (up to 1 year), safety, and tolerability of 2 subcutaneous secukinumab dose regimens in adult patients with moderate to severe hidradenitis suppurativa (SUNSHINE).

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase III

Study Start/End Dates

Study Start Date: January 31, 2019

Primary Completion Date: October 01, 2021
Study Completion Date: July 26, 2022

Study Design/Methodology

This was a multicenter, randomized, double-blind, placebo-controlled, parallel group study with two secukinumab dose regimens (Secukinumab 300mg every 2 weeks, an Secukinumab 300mg every 4 weeks) in 541 subjects with moderate to severe HS.

The study consisted of: Screening (up to 4 weeks), placebo-controlled Treatment Period 1 (16 weeks) and Treatment Period 2 (36 weeks). Subjects who prematurely discontinued the study, or who completed the study and could not or did not wish to continue in the optional extension study, were required to complete a post-treatment follow-up period (8 weeks).

Placebo patients switched to one of the active drug regimens at week 16.

All subjects received a single s.c. injection of blinded study drug (active drug or placebo) once a week for four weeks (induction) at Baseline, Week 1, 2, 3 and 4. Thereafter, the frequency of study drug injections was every 2 weeks for all subjects in order to maintain the treatment blind: either placebo (placebo to secukinumab arms), or secukinumab alternating with placebo every 2 weeks (secukinumab 300 mg every 4 weeks arm) or secukinumab every 2 weeks (secukinumab 300 mg every 2 weeks arm).

Centers

111 centers in 29 countries: United Kingdom(6), Hungary(2), United States(18), Spain(6), Japan(6), Russia(4), Australia(3), India(4), Korea, Republic of(3), Germany(8), Portugal(4), Poland(3), Greece(2), Czech Republic(2), Italy(4), Switzerland(2), Belgium(1), Austria(2), Israel(2), Canada(3), France(8), Taiwan(2), Slovakia (Slovak Republic)(2), Turkey(3), Bulgaria(2), Sweden(1), Argentina(3), Philippines(3), Mexico(2)

Objectives:

The primary objective of this study was to demonstrate the efficacy of secukinumab compared to placebo with respect to

Proportion of patients with Hidradenitis Suppurativa Clinical Response (HiSCR) after 16 weeks of treatment.

The secondary objectives were to demonstrate the efficacy of secukinumab compared to placebo after 16 weeks of treatment with respect to

- Mean percentage change from baseline in AN count at Week 16
- Proportion of patients with hidradenitis suppurativa (HS) flares
- Proportion of patients with clinical response in HS-related skin pain (Numerical rating scale [NRS30])

Test Product, Dose, and Mode of Administration

Secukinumab 300 mg, solution for subcutaneous injection in a; 2mL pre-filled syringe once every 2 weeks; or once every 4 weeks

Placebo solution for subcutaneous injection in a; 2mL pre-filled syringe

Statistical Methods

Treatments

The number of active and placebo injections were summarized by treatment group by means of contingency tables.

The duration of exposure to study treatment was also summarized by treatment group. In addition, the number of subjects with exposure of at least certain thresholds (e.g., any exposure, ≥1 week, ≥2 weeks, ≥3 weeks, ≥4 weeks, ≥8 weeks, etc.) is displayed. Prior and concomitant treatments were summarized by treatment group in separate tables for the Safety Set.

The statistical hypothesis for the primary endpoint (HiSCR50) was that there was no difference in the proportion of subjects achieving HiSCR50 at Week 16 in any of the secukinumab regimens versus placebo regimen.

- H1: secukinumab 300 mg Q2W s.c. is not different to placebo regimen with respect to HiSCR50 after 16 weeks of treatment;
- H2: secukinumab 300 mg Q4W s.c. is not different to placebo regimen with respect to HiSCR50 after 16 weeks of treatment.

The primary analysis method was logistic regression with treatment group, Hurley stage, baseline AN count, geographical region, use of antibiotics and baseline body weight (categorized as stratified) as explanatory variables. Odds ratios were computed for comparisons of secukinumab dose regimens versus placebo.

The analysis method for the secondary endpoint percentage change from baseline in AN count at Week 16 was an ANCOVA model with treatment group, Hurley stage, baseline AN count, geographical region, use of antibiotic and baseline body weight as explanatory variables. The analysis method for the other two secondary endpoints were logistic regression:

- Flare over 16 weeks: with treatment group, Hurley stage, baseline AN count, geographical region, use of antibiotic and baseline body weight (categorized as stratified) as explanatory variables.

- NRS30 (skin pain) at Week 16: with treatment group, Hurley stage, baseline NRS, geographical region, use of antibiotic, baseline body weight (categorized as stratified) as explanatory variables.

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Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Written informed consent must be obtained before any assessment is performed.
- Male and female patients ≥ 18 years of age.
- Diagnosis of HS ≥ 1 year prior to baseline.
- Patients with moderate to severe HS defined as:
- A total of at least 5 inflammatory lesions, i.e. abscesses and/or inflammatory nodules
  AND
- Inflammatory lesions should affect at least 2 distinct anatomic areas
- Patients agree to daily use of topical over-the-counter antiseptics on the areas affected by HS lesions while on study treatment.

Exclusion Criteria:

- Total fistulae count ≥ 20 at baseline.

- Any other active skin disease or condition that may interfere with assessment of HS.
- Active ongoing inflammatory diseases other than HS that require treatment with prohibited medications.
- Use or planned use of prohibited treatment. Washout periods detailed in the protocol have to be adhered to.
- History of hypersensitivity to any of the study drug constituents.
- 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).
- Pregnant or lactating women.

Participant Flow Table

Overall Study

	secukinumab 1 - Q2W	secukinumab 2 - Q4W	placebo	Total
Arm/Group Description	Secukinumab 300mg every 2 weeks	Secukinumab 300mg every 4 weeks	Placebo group to secukinumab 300mg	
Started	181	180	180	541
Completed	168	169	172	509
Not Completed	13	11	8	32
Adverse Event	4	0	1	5
Lost to Follow-up	3	1	1	5
Physician Decision	1	1	1	3
Technical problems	1	0	0	1
Withdrawal by Subject	4	9	5	18

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Baseline Characteristics

	secukinumab 1 - Q2W	secukinumab 2 - Q4W	Placebo	Total
Arm/Group Description	Secukinumab 300mg every 2 weeks	Secukinumab 300mg every 4 weeks	Placebo group to secukinumab 300mg every 4 weeks	
Number of Participants [units: participants]	181	180	180	541
Baseline Analysis Population Description				
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation				
	37.1±12.53	35.7±11.71	35.5±10.75	36.1±11.69
Age Categorical (units: participants) Analysis Population Type: Participants Count of Participants				
<=18 years	0	0	0	0
Between 18 and 65 years	178	177	179	534
>=65 years	3	3	1	7
Race/Ethnicity, Customized (units: participants) Analysis Population Type: Participants Count of Participants				
White	145	146	139	430
Black or African American	15	10	12	37
Asian	19	23	24	66
American Indian or Alaska Native	1	1	2	4
Multiple	1	0	3	4
Sex: Female, Male				

(units: participants)
Analysis Population Type: Participants
Count of Participants

Female	102	100	102	304
Male	79	80	78	237

Summary of Efficacy

Primary Outcome Results

Number of participants with Hidradenitis Suppurativa clinical response (HiSCR)

Description	HiSCR at Week 16 is defined as at least a 50% decrease in Abscess and inflammatory Nodule (AN) count compared to baseline with no increase in the number of abscesses and/or in the number of draining fistulas from baseline to Week 16. The baseline is defined as the last assessment (including unscheduled visits) obtained before/on the day of the first administration of the study treatment, or on the randomization date if there had been no drug administration. The primary endpoint was analyzed by logistic regression. Missing data were multiply imputed based on the estimand strategy related to intercurrent events or missing at random assumption for all missing values not related to intercurrent events. The number of participants reported in this record corresponds to the rounded average number of participants with response in 100 imputed data sets.
Time Frame	Baseline, 16 weeks
Analysis Population Description	Full analysis set (FAS) consisted of all subjects to whom study treatment had been assigned.

	secukinumab 1 - Q2W	**secukinumab 2 - Q4W**	**placebo**
Arm/Group Description	Secukinumab 300mg every 2 weeks	Secukinumab 300mg every 4 weeks	Placebo group to secukinumab 300mg
Number of Participants Analyzed [units: participants]	181	180	180
Number of participants with Hidradenitis Suppurativa clinical response (HiSCR) (units: Rounded average number of participants)			
	81.5 (45.0%)	75.2 (41.8%)	60.7 (45.0%)

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Statistical Analysis

Groups	secukinumab 1 - Q2W, placebo	Logistic regression analysis of HiSCR50 response at Week 16 (multiple imputation)
Type of Statistical Test	Superiority	
P Value	0.0070	
Method	Regression, Logistic multiple imputation	
Odds Ratio, log	1.75	
95% Confidence Interval 2-Sided	1.12 to 2.73	

Statistical Analysis

Groups	secukinumab 2 - Q4W, placebo	Logistic regression analysis of HiSCR50 response at Week 16 (multiple imputation)
Type of Statistical Test	Superiority	
P Value	0.0418	
Method	Regression, Logistic	
Odds Ratio (OR)	1.48	
95% Confidence Interval 2-Sided	0.95 to 2.32	

Secondary Outcome Results

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Percentage change from baseline in AN count at Week 16

Description: The HS affected areas, e.g. right and left axillary (armpit), right and left gluteal ("buttock"), right and left inguinal-femoral (groin), perineal, pubic, sternal, right and left sub-mammary (breast) and others were assessed by the physician for abscesses, inflammatory nodules, draining fistulas, total fistulas, and other lesions. Inflammatory lesions, including abscesses, nodules, draining fistulae, total fistulae and other lesions were counted. The analysis method for percentage change from baseline in abscesses and inflammatory nodules (AN) count at Week 16 was an ANCOVA model.

Time Frame: Baseline, 16 weeks

Analysis Population Description: FAS

	secukinumab 1 - Q2W	secukinumab 2 - Q4W	placebo
Arm/Group Description	Secukinumab 300mg every 2 weeks	Secukinumab 300mg every 4 weeks	Placebo group to secukinumab 300mg
Number of Participants Analyzed [units: participants]	181	180	180
Percentage change from baseline in AN count at Week 16 (units: percentage change from baseline)	**Mean ± Standard Error**	**Mean ± Standard Error**	**Mean ± Standard Error**
	-46.8 ± 3.33	-42.4 ± 4.01	-24.3 ± 4.33

Statistical Analysis

Groups	secukinumab 1 - Q2W, placebo	Analysis of covariance of percentage change from baseline in AN count at Week 16 (multiple imputation)
Type of Statistical Test	Superiority	
P Value	<0.0001	
Method	ANCOVA	

Least square Mean Difference	-23.05
95% Confidence Interval 2-Sided	-33.90 to -12.21

Statistical Analysis

Groups	secukinumab 2 - Q4W, placebo	Analysis of covariance of percentage change from baseline in AN count at Week 16 (multiple imputation)
Type of Statistical Test	Superiority	
P Value	0.0004	
Method	ANCOVA	
Least Square Mean difference	-18.46	
95% Confidence Interval 2-Sided	-29.32 to -7.60	

Number of participants with Hidradenitis Suppurativa (HS) flares

Description	Flare was defined as at least a 25% increase in AN count with a minimum increase of 2 AN compared to baseline. The proportion of patients with HS flares was analyzed by logistic regression. The number of participants reported in this record corresponds to the rounded average number of participants with response in 100 imputed data sets
Time Frame	Baseline, 16 weeks
Analysis Population Description	FAS

	secukinumab 1 - Q2W	**secukinumab 2 - Q4W**	**placebo 2**
Arm/Group Description	Secukinumab 300mg every 2 weeks	Secukinumab 300mg every 4 weeks	Placebo group to secukinumab 300mg
Number of Participants Analyzed [units: participants]	181	180	180

Number of participants with Hidradenitis Suppurativa (HS) flares
(units: Rounded average number of participants)

	27.8 (15.4%)	41.7 (23.2%)	52.2 (15.4%)

Statistical Analysis

Groups	secukinumab 1 - Q2W, placebo 2	Logistic regression analysis of Flare over 16 weeks (multiple imputation)
Type of Statistical Test	Superiority	
P Value	0.0010	
Method	Regression, Logistic	
Odds Ratio, log	0.42	
95% Confidence Interval 2-Sided	0.25 to 0.73	

Statistical Analysis

Groups	secukinumab 2 - Q4W, placebo 2	Logistic regression analysis of Flare over 16 weeks (multiple imputation)
Type of Statistical Test	Superiority	
P Value	0.0926	
Method	Regression, Logistic	
Odds Ratio (OR)	0.71	
95% Confidence Interval 2-Sided	0.43 to 1.17	

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Number of participants achieving NRS30 (Skin pain)

Description	The Patient's global assessment of skin pain - numerical rating scale (NRS) in the past 24 hours was used to assess pain “at its worst” and the average skin pain due to HS in the last 24 hours. The NRS is a segmented numeric version of the visual analog scale in which a respondent selects a whole number (0–10 integers) that best reflects the intensity of their pain ranging from 0 (no skin pain) to 10 (skin pain as bad as you can imagine). NRS30 (skin pain) was defined as at least a 30% reduction and at least 2 units reduction from baseline in Patient's Global Assessment of Skin Pain - at worst. This endpoint was analyzed by logistic regression. The number of participants reported in this record corresponds to the rounded average number of participants with response in 100 imputed data sets.
Time Frame	Baseline, 16 weeks
Analysis Population Description	FAS

	secukinumab 1 - Q2W	secukinumab 2 - Q4W	placebo
Arm/Group Description	Secukinumab 300mg every 2 weeks	Secukinumab 300mg every 4 weeks	Placebo group to secukinumab 300mg
Number of Participants Analyzed [units: participants]	131	123	119
Participants achieving NRS30 (units: rounded average number of participants)			
	44.7 (34.1%)	39.7 (32.2%)	28.3 (23.8%)

Statistical Analysis

Groups	secukinumab 1 - Q2W, placebo	Logistic regression analysis of skin pain/NRS30 response at Week 16 (pooled data, multiple imputation)
Type of Statistical Test	Superiority	
P Value	0.0003	
Method	Regression, Logistic	

Odds Ratio (OR)	2.08
95% Confidence Interval 2-Sided	1.37 to 3.16

Statistical Analysis

Groups	secukinumab 2 - Q4W, placebo	Logistic regression analysis of skin pain/NRS30 response at Week 16 (pooled data, multiple imputation)
Type of Statistical Test	Superiority	
P Value	0.0044	
Method	Regression, Logistic	
Odds Ratio, log	1.77	
95% Confidence Interval 2-Sided	1.15 to 2.70	

No data identified.

Summary of Safety

Safety Results

Time Frame	Adverse events (AEs) were reported from first dose of study treatment, up to approximately 60 weeks for AIN457 (up to 52 weeks for subjects moving to extension study) and 16 weeks for placebo.
Additional Description	AEs are any sign or symptom that occurs during the conduct of the trial and safety follow-up.
Source Vocabulary for Table Default	MedDRA (25.0)

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Collection Approach for Table Default Systematic Assessment

All-Cause Mortality

	AIN457 Q2W N = 181	AIN457 Q4W N = 180	Placebo N = 180	Any AIN457 Q2W N = 266	Any AIN457 Q4W N = 267	Any AIN457 N = 533
Arm/Group Description	Subjects who were randomized to AIN457 (secukinumab) 300mg Q2W dose regimen at the study entry. Adverse events were assessed up to Week 52	Subjects who were randomized to AIN457 (secukinumab) 300mg Q4W dose regimen at the study entry. Adverse events were assessed up to Week 52	Subjects received matching placebo up to 16 weeks	Subjects who received at least 1 dose of secukinumab 300 mg Q2W dose (e.g., subjects who switched from placebo to secukinumab Q2W at Week 16). Adverse events were assessed up to Week 52	Subjects who received at least 1 dose of secukinumab 300 mg Q4W dose (e.g., subjects who switched from placebo to secukinumab Q4W at Week 16). Adverse events were assessed up to Week 52	Subjects who received at least 1 dose of secukinumab
Total Number Affected	0	0	0	0	0	0
Total Number At Risk	181	180	180	266	267	533

Serious Adverse Events

	AIN457 Q2W N = 181	AIN457 Q4W N = 180	Placebo N = 180	Any AIN457 Q2W N = 266	Any AIN457 Q4W N = 267	Any AIN457 N = 533
Arm/Group Description	Subjects who were randomized to AIN457 (secukinumab) 300mg Q2W dose	Subjects who were randomized to AIN457 (secukinumab) 300mg Q4W dose	Subjects received matching placebo up to 16 weeks	Subjects who received at least 1 dose of secukinumab 300 mg Q2W dose	Subjects who received at least 1 dose of secukinumab 300 mg Q4W dose	Subjects who received at least 1 dose of secukinumab

	regimen at the study entry. Adverse events were assessed up to Week 52	regimen at the study entry. Adverse events were assessed up to Week 52		(e.g., subjects who switched from placebo to secukinumab Q2W at Week 16). Adverse events were assessed up to Week 52	(e.g., subjects who switched from placebo to secukinumab Q4W at Week 16). Adverse events were assessed up to Week 52	
Total # Affected by any Serious Adverse Event	13	9	6	18	19	37
Total # at Risk by any Serious Adverse Event	181	180	180	266	267	533
Cardiac disorders						
Pericarditis	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Gastrointestinal disorders						
Abdominal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Constipation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Diarrhoea haemorrhagic	0 (0.00%)	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Inguinal hernia	1 (0.55%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Vomiting	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
General disorders and administration site conditions						
Fatigue	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Pyrexia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Infections and infestations						
Appendicitis	0 (0.00%)	1 (0.56%)	0 (0.00%)	1 (0.38%)	1 (0.37%)	2 (0.38%)
Breast cellulitis	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)

Cellulitis	1 (0.55%)	1 (0.56%)	0 (0.00%)	1 (0.38%)	1 (0.37%)	2 (0.38%)
Clostridium difficile colitis	0 (0.00%)	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
COVID-19	1 (0.55%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.37%)	2 (0.38%)
Infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Influenza	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Large intestine infection	1 (0.55%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Peritonsillar abscess	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.75%)	2 (0.38%)
Post procedural infection	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Sepsis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Skin candida	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Sweat gland infection	1 (0.55%)	3 (1.67%)	0 (0.00%)	1 (0.38%)	3 (1.12%)	4 (0.75%)
Urinary tract infection	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Injury, poisoning and procedural complications						
Foot fracture	0 (0.00%)	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Meniscus injury	1 (0.55%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Musculoskeletal and connective tissue disorders						
Foot deformity	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Lung cancer metastatic	0 (0.00%)	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Non-small cell lung cancer metastatic	1 (0.55%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Nervous system disorders						

Dizziness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Headache	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Sciatica	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Psychiatric disorders						
Suicidal ideation	1 (0.55%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Suicide attempt	1 (0.55%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Renal and urinary disorders						
C3 glomerulopathy	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Ureterolithiasis	0 (0.00%)	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders						
Pulmonary embolism	1 (0.55%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Sleep apnoea syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Skin and subcutaneous tissue disorders						
Hidradenitis	3 (1.66%)	3 (1.67%)	2 (1.11%)	4 (1.50%)	4 (1.50%)	8 (1.50%)
Vascular disorders						
Hypertensive emergency	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.37%)	1 (0.19%)
Thrombosis	1 (0.55%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)

Other (Not Including Serious) Adverse Events

Frequent Event Reporting Threshold 2%

	AIN457 Q2W N = 181	AIN457 Q4W N = 180	Placebo N = 180	Any AIN457 Q2W N = 266	Any AIN457 Q4W N = 267	Any AIN457 N = 533
Arm/Group Description	Subjects who were randomized to AIN457 (secukinumab) 300mg Q2W dose regimen at the study entry. Adverse events were assessed up to Week 52	Subjects who were randomized to AIN457 (secukinumab) 300mg Q4W dose regimen at the study entry. Adverse events were assessed up to Week 52	Subjects received matching placebo up to 16 weeks	Subjects who received at least 1 dose of secukinumab 300 mg Q2W dose (e.g., subjects who switched from placebo to secukinumab Q2W at Week 16). Adverse events were assessed up to Week 52	Subjects who received at least 1 dose of secukinumab 300 mg Q4W dose (e.g., subjects who switched from placebo to secukinumab Q4W at Week 16). Adverse events were assessed up to Week 52	Subjects who received at least 1 dose of secukinumab
Total # Affected by any Other Adverse Event	135	132	88	184	183	367
Total # at Risk by any Other Adverse Event	181	180	180	266	267	533
Gastrointestinal disorders						
Abdominal pain	7 (3.87%)	6 (3.33%)	1 (0.56%)	8 (3.01%)	10 (3.75%)	18 (3.38%)
Abdominal pain upper	4 (2.21%)	5 (2.78%)	1 (0.56%)	4 (1.50%)	9 (3.37%)	13 (2.44%)
Constipation	1 (0.55%)	5 (2.78%)	0 (0.00%)	1 (0.38%)	5 (1.87%)	6 (1.13%)
Diarrhoea	11 (6.08%)	16 (8.89%)	9 (5.00%)	12 (4.51%)	24 (8.99%)	36 (6.75%)
Nausea	4 (2.21%)	8 (4.44%)	7 (3.89%)	6 (2.26%)	13 (4.87%)	19 (3.56%)
Toothache	7 (3.87%)	6 (3.33%)	4 (2.22%)	9 (3.38%)	7 (2.62%)	16 (3.00%)
Vomiting	5 (2.76%)	7 (3.89%)	0 (0.00%)	6 (2.26%)	9 (3.37%)	15 (2.81%)
General disorders and administration site conditions						
Asthenia	3 (1.66%)	4 (2.22%)	4 (2.22%)	5 (1.88%)	4 (1.50%)	9 (1.69%)
Chest pain	0 (0.00%)	5 (2.78%)	0 (0.00%)	0 (0.00%)	5 (1.87%)	5 (0.94%)

Fatigue	6 (3.31%)	11 (6.11%)	8 (4.44%)	8 (3.01%)	13 (4.87%)	21 (3.94%)
Pyrexia	13 (7.18%)	8 (4.44%)	2 (1.11%)	16 (6.02%)	12 (4.49%)	28 (5.25%)
Hepatobiliary disorders						
Hepatic steatosis	4 (2.21%)	2 (1.11%)	2 (1.11%)	4 (1.50%)	3 (1.12%)	7 (1.31%)
Infections and infestations						
Bronchitis	5 (2.76%)	6 (3.33%)	3 (1.67%)	5 (1.88%)	8 (3.00%)	13 (2.44%)
Cellulitis	4 (2.21%)	3 (1.67%)	4 (2.22%)	6 (2.26%)	6 (2.25%)	12 (2.25%)
Conjunctivitis	5 (2.76%)	4 (2.22%)	1 (0.56%)	5 (1.88%)	6 (2.25%)	11 (2.06%)
COVID-19	5 (2.76%)	3 (1.67%)	0 (0.00%)	6 (2.26%)	7 (2.62%)	13 (2.44%)
Ear infection	3 (1.66%)	4 (2.22%)	0 (0.00%)	3 (1.13%)	4 (1.50%)	7 (1.31%)
Folliculitis	4 (2.21%)	4 (2.22%)	2 (1.11%)	6 (2.26%)	4 (1.50%)	10 (1.88%)
Fungal skin infection	4 (2.21%)	0 (0.00%)	0 (0.00%)	4 (1.50%)	0 (0.00%)	4 (0.75%)
Gastroenteritis	8 (4.42%)	4 (2.22%)	1 (0.56%)	8 (3.01%)	4 (1.50%)	12 (2.25%)
Influenza	1 (0.55%)	6 (3.33%)	4 (2.22%)	1 (0.38%)	6 (2.25%)	7 (1.31%)
Nasopharyngitis	32 (17.68%)	24 (13.33%)	13 (7.22%)	40 (15.04%)	29 (10.86%)	69 (12.95%)
Pharyngitis	7 (3.87%)	5 (2.78%)	1 (0.56%)	8 (3.01%)	7 (2.62%)	15 (2.81%)
Sinusitis	4 (2.21%)	2 (1.11%)	2 (1.11%)	7 (2.63%)	2 (0.75%)	9 (1.69%)
Suspected COVID-19	5 (2.76%)	3 (1.67%)	0 (0.00%)	6 (2.26%)	7 (2.62%)	13 (2.44%)
Tonsillitis	6 (3.31%)	2 (1.11%)	1 (0.56%)	7 (2.63%)	4 (1.50%)	11 (2.06%)
Upper respiratory tract infection	9 (4.97%)	13 (7.22%)	4 (2.22%)	12 (4.51%)	17 (6.37%)	29 (5.44%)
Urinary tract infection	9 (4.97%)	8 (4.44%)	3 (1.67%)	10 (3.76%)	10 (3.75%)	20 (3.75%)
Vulvovaginal candidiasis	4 (2.21%)	2 (1.11%)	0 (0.00%)	4 (1.50%)	3 (1.12%)	7 (1.31%)
Vulvovaginal mycotic infection	6 (3.31%)	2 (1.11%)	1 (0.56%)	7 (2.63%)	4 (1.50%)	11 (2.06%)
Injury, poisoning and procedural complications						

Ligament sprain	6 (3.31%)	4 (2.22%)	0 (0.00%)	8 (3.01%)	4 (1.50%)	12 (2.25%)
Investigations						
Amylase increased	3 (1.66%)	4 (2.22%)	0 (0.00%)	3 (1.13%)	5 (1.87%)	8 (1.50%)
Lipase increased	8 (4.42%)	7 (3.89%)	2 (1.11%)	8 (3.01%)	9 (3.37%)	17 (3.19%)
SARS-CoV-2 test negative	6 (3.31%)	5 (2.78%)	2 (1.11%)	8 (3.01%)	7 (2.62%)	15 (2.81%)
SARS-CoV-2 test positive	2 (1.10%)	4 (2.22%)	0 (0.00%)	4 (1.50%)	5 (1.87%)	9 (1.69%)
Weight increased	2 (1.10%)	5 (2.78%)	2 (1.11%)	3 (1.13%)	5 (1.87%)	8 (1.50%)
White blood cell count increased	1 (0.55%)	2 (1.11%)	4 (2.22%)	3 (1.13%)	2 (0.75%)	5 (0.94%)
Metabolism and nutrition disorders						
Hyperuricaemia	4 (2.21%)	3 (1.67%)	0 (0.00%)	4 (1.50%)	3 (1.12%)	7 (1.31%)
Musculoskeletal and connective tissue disorders						
Arthralgia	11 (6.08%)	6 (3.33%)	8 (4.44%)	14 (5.26%)	9 (3.37%)	23 (4.32%)
Back pain	7 (3.87%)	8 (4.44%)	8 (4.44%)	7 (2.63%)	12 (4.49%)	19 (3.56%)
Pain in extremity	3 (1.66%)	4 (2.22%)	5 (2.78%)	5 (1.88%)	5 (1.87%)	10 (1.88%)
Nervous system disorders						
Dizziness	6 (3.31%)	3 (1.67%)	3 (1.67%)	7 (2.63%)	5 (1.87%)	12 (2.25%)
Headache	33 (18.23%)	32 (17.78%)	14 (7.78%)	39 (14.66%)	46 (17.23%)	85 (15.95%)
Migraine	5 (2.76%)	1 (0.56%)	0 (0.00%)	5 (1.88%)	3 (1.12%)	8 (1.50%)
Psychiatric disorders						
Depression	4 (2.21%)	2 (1.11%)	2 (1.11%)	6 (2.26%)	3 (1.12%)	9 (1.69%)
Reproductive system and breast disorders						
Dysmenorrhoea	1 (0.55%)	1 (0.56%)	4 (2.22%)	2 (0.75%)	4 (1.50%)	6 (1.13%)

Respiratory, thoracic and mediastinal disorders						
Cough	4 (2.21%)	8 (4.44%)	1 (0.56%)	7 (2.63%)	10 (3.75%)	17 (3.19%)
Oropharyngeal pain	9 (4.97%)	5 (2.78%)	3 (1.67%)	11 (4.14%)	7 (2.62%)	18 (3.38%)
Rhinorrhoea	8 (4.42%)	2 (1.11%)	2 (1.11%)	9 (3.38%)	4 (1.50%)	13 (2.44%)
Skin and subcutaneous tissue disorders						
Acne	4 (2.21%)	5 (2.78%)	2 (1.11%)	5 (1.88%)	6 (2.25%)	11 (2.06%)
Dermatitis	3 (1.66%)	4 (2.22%)	1 (0.56%)	4 (1.50%)	5 (1.87%)	9 (1.69%)
Dermatitis contact	3 (1.66%)	6 (3.33%)	0 (0.00%)	3 (1.13%)	6 (2.25%)	9 (1.69%)
Eczema	8 (4.42%)	6 (3.33%)	1 (0.56%)	9 (3.38%)	9 (3.37%)	18 (3.38%)
Hidradenitis	16 (8.84%)	17 (9.44%)	23 (12.78%)	28 (10.53%)	26 (9.74%)	54 (10.13%)
Intertrigo	10 (5.52%)	7 (3.89%)	2 (1.11%)	11 (4.14%)	8 (3.00%)	19 (3.56%)
Pruritus	11 (6.08%)	6 (3.33%)	2 (1.11%)	15 (5.64%)	8 (3.00%)	23 (4.32%)
Psoriasis	6 (3.31%)	5 (2.78%)	1 (0.56%)	6 (2.26%)	5 (1.87%)	11 (2.06%)
Rash	4 (2.21%)	4 (2.22%)	1 (0.56%)	6 (2.26%)	5 (1.87%)	11 (2.06%)
Seborrhoeic dermatitis	4 (2.21%)	5 (2.78%)	2 (1.11%)	6 (2.26%)	6 (2.25%)	12 (2.25%)
Vascular disorders						
Hypertension	6 (3.31%)	4 (2.22%)	2 (1.11%)	8 (3.01%)	5 (1.87%)	13 (2.44%)

Conclusion

The efficacy was demonstrated by both dose regimens of secukinumab dosed every-other-week (Q2W) and every 4 weeks (Q4W) compared to placebo at Week 16 although only the Q2W regimen met the primary and all secondary endpoints in the pre-defined hypothesis testing hierarchy. Further, a trend for improvement in HiSCR50, AN count, Flare and Skin Pain (NRS30) beyond the Week 16 timepoint was observed. Secukinumab was safe and well-tolerated for long-

term (52 weeks) use in adult subjects with moderate to severe hidradenitis suppurativa (HS), showing comparable safety profiles between both secukinumab dose regimens. No new or unexpected safety signals were observed with long-term treatment with either dosing regimen of secukinumab. In addition, in subjects with HS, the safety profiles of the secukinumab Q2W or Q4W dosing regimens were consistent with the previously described safety profile of secukinumab across other approved indications.

Date of Clinical Trial Report

December 20, 2022