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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Secukinumab

Trial Indication(s)

hidradenitis suppurativa (HS)

Protocol Number

CAIN457M2302

Protocol Title

A randomized, double-blind, multicenter 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 (SUNRISE)

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase III

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Study Start/End Dates

Study Start Date: February 25, 2019 (Actual)
Primary Completion Date: September 23, 2021 (Actual)
Study Completion Date: July 19, 2022 (Actual)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This was a multicenter, randomized, double-blind, placebo-controlled, parallel group study with two secukinumab dose regimens in 543 subjects with moderate to severe HS.

The study consisted of: Screening Period (up to 4 weeks), placebo-controlled Treatment Period 1 (16 weeks) and Treatment Period 2 (36 weeks).

In Treatment Period 1 patients were randomly assigned (1:1:1) to receive subcutaneous secukinumab 300 mg every 2 weeks (AIN457 Q2W), subcutaneous secukinumab 300 mg every 4 weeks (AIN457 Q4W), or subcutaneous placebo all via a 2 mL prefilled syringe in a double-dummy method as per treatment assignment.

In Treatment Period 2 Placebo patients were re-randomized to one of the active drug regimens at week 16.

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).

Centers

108 centers in 32 countries: United States(15), United Kingdom(6), Germany(10), Spain(6), Hungary(3), Russia(3), Denmark(2), Lithuania(2), Greece(2), India(2), Singapore(3), South Africa(2), Slovakia (Slovak Republic)(2), Belgium(2), Czech Republic(2), Poland(3), Turkey(4), Israel(2), France(9), Italy(4), Canada(4), Vietnam(2), Bulgaria(2),

Switzerland(2), Netherlands(1), Malaysia(3), Argentina(3), Philippines(1), Guatemala(2), Colombia(2), Lebanon(1), Croatia(1)

Objectives:

The primary objective of this study was to demonstrate the efficacy of secukinumab compared to placebo with respect to Hidradenitis Suppurativa Clinical Response (HiSCR50) 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

- Percentage change from baseline in Abscess and Inflammatory Nodule (AN) count
- 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 (s), Dose(s), and Mode(s) 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

The statistical hypothesis for the primary endpoint (HiSCR50 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) 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 counts, 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.

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

Treatment Period 1 (until week 16)

	AIN457 Q2W	AIN457 Q4W	Placebo	Placebo - Re-randomized to AIN457 Q2W	Placebo - Re-randomized to AIN457 Q4W	Total
Arm/Group Description	Secukinumab 300mg every 2 weeks (Treatment Period 1 and 2)	Secukinumab 300mg every 4 weeks (Treatment Period 1 and 2)	Placebo group to secukinumab 300mg (Treatment Period 1)	Placebo group, re-randomized to secukinumab 300mg Q2W at week 16 (Treatment Period 2)	Placebo group, re-randomized to secukinumab 300mg Q4W at week 16 (Treatment Period 2)	
Started	181[1]	180	183	0	0	544
Full Analysis Set	180	180	183	0	0	543
Completed	170	169	167	0	0	506
Not Completed	11	11	16	0	0	38
Withdrawal by Subject	6	6	8	0	0	20
Adverse Event	1	4	4	0	0	9
Lost to Follow-up	1	1	1	0	0	3
Lack of Efficacy	1	0	1	0	0	2

Technical problems	1	0	1	0	0	2
Pregnancy	0	0	1	0	0	1
Misrandomized Subject	1	0	0	0	0	1

[1] 1 patient was mis randomized and excluded from the full analysis set.

Treatment Period 2 (after week 16)

	AIN457 Q2W	AIN457 Q4W	Placebo	Placebo - Re-randomized to AIN457 Q2W	Placebo - Re-randomized to AIN457 Q4W	Total
Arm/Group Description	Secukinumab 300mg every 2 weeks (Treatment Period 1 and 2)	Secukinumab 300mg every 4 weeks (Treatment Period 1 and 2)	Placebo group to secukinumab 300mg (Treatment Period 1)	Placebo group, re-randomized to secukinumab 300mg Q2W at week 16 (Treatment Period 2)	Placebo group, re-randomized to secukinumab 300mg Q4W at week 16 (Treatment Period 2)	
Started	170	169	0	81	86	506
Completed	149	133	0	68	69	419
Not Completed	21	36	0	13	17	87
Withdrawal by Subject	9	18	0	9	12	48
Adverse Event	6	3	0	2	1	12
Lack of Efficacy	3	3	0	1	2	9
Lost to Follow-up	1	8	0	1	0	10
Physician Decision	1	2	0	0	2	5
Technical Problems	1	0	0	0	0	1
Death	0	1	0	0	0	1
Pregnancy	0	1	0	0	0	1

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Baseline Characteristics

	AIN457 Q2W	AIN457 Q4W	Placebo	Total
Arm/Group Description	Secukinumab 300mg every 2 weeks	Secukinumab 300mg every 4 weeks	Placebo group to secukinumab 300mg	
Number of Participants [units: participants]	180	180	183	543
Baseline Analysis Population Description	Full Analysis Set (FAS)			
Age Categorical (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)				
Group 1 : <=18 years	0	0	0	0
Group 1 : Between 18 and 65 years	177	178	181	536
Group 1 : >=65 years	3	2	2	7
Age Continuous (units: Years) Analysis Population Type: Participants Mean ± Standard Deviation				
	37.3±11.48	35.5±11.41	36.2±11.25	36.3±11.38
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)				
Female	98	103	105	306
Male	82	77	78	237
Race/Ethnicity, Customized (units: Participants)				

Analysis Population Type: Participants
Count of Participants (Not Applicable)

Race : White	133	139	143	415
Race : Black or African American	18	19	12	49
Race : Asian	16	16	19	51
Race : Native Hawaiian or Other Pacific Islander	1	0	0	1
Race : American Indian or Alaska native	7	5	8	20
Race : Multiple	4	1	1	6
Race : Not Reported	1	0	0	1

Primary Outcome Result(s)

Percentage of participants with Hidradenitis Suppurativa Clinical Response (HiSCR50)

Description	HiSCR50 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. This endpoint was analyzed by logistic regression.
Time Frame	16 weeks
Analysis Population Description	Full analysis set (FAS): consisted of all subjects to whom study treatment had been assigned, excluding mis-randomized patients. Subjects were analyzed according to the treatment assigned at randomization.

	AIN457 Q2W	AIN457 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]	180	180	183
Percentage of participants with Hidradenitis Suppurativa Clinical Response (HiSCR50) (units: Percentage of Participants)			
	42.3	46.1	31.2

Statistical Analysis

Groups	AIN457 Q2W, Placebo	
Type of Statistical Test	Superiority	
P Value	0.0149	one-sided p-value
Method	Regression, Logistic	
Odds Ratio (OR)	1.64	
95 % Confidence Interval 2-Sided	1.05 to 2.55	

Statistical Analysis

Groups	AIN457 Q4W, Placebo	
Type of Statistical Test	Superiority	
P Value	0.0022	one-sided p-value
Method	Regression, Logistic	
Odds Ratio (OR)	1.90	

95 % Confidence Interval 2-Sided	1.22 to 2.96

Secondary Outcome Result(s)

Percentage change from baseline in AN count

Description	Percent change from baseline in abscesses and inflammatory nodules (AN) count. This endpoint was analyzed by analysis of covariance.
Time Frame	Baseline, 16 weeks
Analysis Population Description	Full Analysis Set

	AIN457 Q2W	AIN457 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]	180	180	183
Percentage change from baseline in AN count (units: Percentage change from baseline)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
	-39.3 ± 4.43	-45.5 ± 4.08	-22.4 ± 4.84

Statistical Analysis

Groups	AIN457 Q2W, Placebo
Type of Statistical Test	Superiority

P Value	0.0051	one-side p-value
Method	ANCOVA	
Mean Difference (Net)	-16.33	
95 % Confidence Interval 2-Sided	-28.79 to -3.88	

Statistical Analysis

Groups	AIN457 Q4W, Placebo	
Type of Statistical Test	Superiority	
P Value	0.0001	one-side p-value
Method	ANCOVA	
Mean Difference (Net)	-22.94	
95 % Confidence Interval 2-Sided	-35.24 to -10.63	

Percentage of participants with Hidradenitis Suppurativa (HS) flares

Description	Percentage of participants who experience at least one flare over 16 weeks. A flare is defined as at least a 25% increase in abscesses and inflammatory nodules (AN) count with a minimum increase of 2 AN relative to baseline. This endpoint was analyzed by logistic regression.
Time Frame	16 weeks
Analysis Population Description	Full Analysis Set

	AIN457 Q2W	AIN457 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]	180	180	183
Percentage of participants with Hidradenitis Suppurativa (HS) flares (units: Percentage of Participants)			
	20.1	15.6	27.0

Statistical Analysis

Groups	AIN457 Q2W, Placebo	
Type of Statistical Test	Superiority	
P Value	0.0732	one-sided p-value
Method	Regression, Logistic	
Odds Ratio (OR)	0.68	
95 % Confidence Interval 2-Sided	0.41 to 1.14	

Statistical Analysis

Groups	AIN457 Q4W, Placebo	
Type of Statistical Test	Superiority	
P Value	0.0049	one-sided p-value

Method	Regression, Logistic
Odds Ratio (OR)	0.49
95 % Confidence Interval 2-Sided	0.29 to 0.84

Percentage of participants achieving NRS30

Description	Patients achieving Numerical Rating Scale score of 30 (NRS30) at week 16, defined as at least a 30% reduction and at least one unit reduction from baseline in the Patient's Global assessment of Skin Pain (where range 0 [no skin pain] to 10 [worst skin pain]). This endpoint was analyzed by logistic regression. The protocol defines this outcome measure to be tested using combined data with CAIN457M2301 (NCT03713619). As this record is supposed to contain only results from CAIN457M2302, descriptive data based only on CAIN457M2302 are presented.
Time Frame	16 weeks
Analysis Population Description	Full Analysis Set restricted to participants with baseline NRS score greater or equal to 3

	AIN457 Q2W	AIN457 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]	135	129	132
Percentage of participants achieving NRS30 (units: Percentage of participants)			
	38.6	34.7	22.4

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Statistical Analysis

Groups	AIN457 Q2W, Placebo	
Type of Statistical Test	Superiority	
P Value	0.0026	one-sided p-value
Method	Regression, Logistic	
Odds Ratio (OR)	2.29	
95 % Confidence Interval 2-Sided	1.28 to 4.09	

Statistical Analysis

Groups	AIN457 Q4W, Placebo	
Type of Statistical Test	Superiority	
P Value	0.0206	one-sided p-value
Method	Regression, Logistic	
Odds Ratio (OR)	1.86	
95 % Confidence Interval 2-Sided	1.03 to 3.37	

Safety Results

Time Frame	Adverse events (AEs) were reported from first dose of study treatment, up to approximately 52 weeks for AIN457 (up to 60 weeks for subjects who did not move to the extension study) and up to 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)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	AIN457 Q2W N = 180	AIN457 Q4W N = 180	Placebo N = 183	Any AIN457 Q2W N = 261	Any AIN457 Q4W N = 266	Any AIN457 N = 527
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 60	Subjects who were randomized to AIN457 (secukinumab) 300mg Q4W dose regimen at the study entry. Adverse events were assessed up to Week 60	Subjects who were randomized to matching placebo at the study entry. Adverse events were assessed up to Week 16	Subjects who received at least 1 dose of secukinumab 300 mg Q2W dose (including subjects who switched from placebo to secukinumab Q2W at Week 16). Adverse events were assessed up to Week 60	Subjects who received at least 1 dose of secukinumab 300 mg Q4W dose (including subjects who switched from placebo to secukinumab Q4W at Week 16). Adverse events were assessed up to Week 60	Subjects who received at least 1 dose of secukinumab

Total Number Affected	0	1	0	0	2	2
Total Number At Risk	180	180	183	261	266	527

Serious Adverse Events

Time Frame	Adverse events (AEs) were reported from first dose of study treatment, up to approximately 52 weeks for AIN457 (up to 60 weeks for subjects who did not move to the extension study) and up to 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)
Collection Approach for Table Default	Systematic Assessment

	AIN457 Q2W N = 180	**AIN457 Q4W N = 180**	**Placebo N = 183**	**Any AIN457 Q2W N = 261**	**Any AIN457 Q4W N = 266**	**Any AIN457 N = 527**
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 60	Subjects who were randomized to AIN457 (secukinumab) 300mg Q4W dose regimen at the study entry. Adverse events were assessed up to Week 60	Subjects who were randomized to matching placebo at the study entry. Adverse events were assessed up to Week 16	Subjects who received at least 1 dose of secukinumab 300 mg Q2W dose (including subjects who switched from placebo to secukinumab Q2W at Week 16). Adverse	Subjects who received at least 1 dose of secukinumab 300 mg Q4W dose (including subjects who switched from placebo to secukinumab Q4W at Week 16). Adverse	Subjects who received at least 1 dose of secukinumab

				events were assessed up to Week 60	events were assessed up to Week 60	
Total # Affected by any Serious Adverse Event	19	15	5	22	23	45
Total # at Risk by any Serious Adverse Event	180	180	183	261	266	527
Cardiac disorders						
Arrhythmia	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Myocardial infarction	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Gastrointestinal disorders						
Colitis ulcerative	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Gastrointestinal haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Inflammatory bowel disease	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
General disorders and administration site conditions						
Pyrexia	2 (1.11%)	0 (0.00%)	1 (0.55%)	2 (0.77%)	0 (0.00%)	2 (0.38%)
Systemic inflammatory response syndrome	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Unevaluable event	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Hepatobiliary disorders						
Cholecystitis	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Cholecystitis acute	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Cholelithiasis	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Immune system disorders						
Amyloidosis	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)

Infections and infestations						
Abscess	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Abscess limb	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Cellulitis	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Clostridium difficile colitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Colonic abscess	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
COVID-19 pneumonia	0 (0.00%)	0 (0.00%)	1 (0.55%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dermatitis infected	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Enterocolitis infectious	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Injection site abscess	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Localised infection	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Otitis externa	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Pyelonephritis	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Scrotal infection	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Soft tissue infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Sweat gland infection	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.38%)	2 (0.38%)
Urinary tract infection	1 (0.56%)	0 (0.00%)	1 (0.55%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Viral upper respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Injury, poisoning and procedural complications						
Ankle fracture	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Fibula fracture	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Intentional overdose	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Joint dislocation	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Lower limb fracture	1 (0.56%)	1 (0.56%)	0 (0.00%)	1 (0.38%)	1 (0.38%)	2 (0.38%)

Skull fracture	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Musculoskeletal and connective tissue disorders						
Intervertebral disc protrusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.75%)	2 (0.38%)
Muscle spasms	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Osteoarthritis	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Basal cell carcinoma	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Breast cancer	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Nervous system disorders						
Sciatica	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Psychiatric disorders						
Confusional state	0 (0.00%)	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)
Depression	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Obsessive-compulsive disorder	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Renal and urinary disorders						
Acute kidney injury	2 (1.11%)	0 (0.00%)	0 (0.00%)	2 (0.77%)	0 (0.00%)	2 (0.38%)
Glomerular vascular disorder	0 (0.00%)	0 (0.00%)	1 (0.55%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nephrolithiasis	1 (0.56%)	1 (0.56%)	0 (0.00%)	1 (0.38%)	1 (0.38%)	2 (0.38%)
Pelvi-ureteric obstruction	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)
Reproductive system and breast disorders						
Scrotal inflammation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	1 (0.19%)

Respiratory, thoracic and mediastinal disorders						
Asthma	0 (0.00%)	0 (0.00%)	1 (0.55%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders						
Hidradenitis	4 (2.22%)	0 (0.00%)	0 (0.00%)	5 (1.92%)	0 (0.00%)	5 (0.95%)
Vascular disorders						
Hypotension	1 (0.56%)	0 (0.00%)	0 (0.00%)	1 (0.38%)	0 (0.00%)	1 (0.19%)

Other (Not Including Serious) Adverse Events

Time Frame	Adverse events (AEs) were reported from first dose of study treatment, up to approximately 52 weeks for AIN457 (up to 60 weeks for subjects who did not move to the extension study) and up to 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)
Collection Approach for Table Default	Systematic Assessment

Frequent Event Reporting Threshold 2%

	AIN457 Q2W N = 180	AIN457 Q4W N = 180	Placebo N = 183	Any AIN457 Q2W N = 261	Any AIN457 Q4W N = 266	Any AIN457 N = 527
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 60	Subjects who were randomized to AIN457 (secukinumab) 300mg Q4W dose regimen at the study entry. Adverse events were assessed up to Week 60	Subjects who were randomized to matching placebo at the study entry. Adverse events were assessed up to Week 16	Subjects who received at least 1 dose of secukinumab 300 mg Q2W dose (including subjects who switched from placebo to secukinumab Q2W at Week 16). Adverse events were assessed up to Week 60	Subjects who received at least 1 dose of secukinumab 300 mg Q4W dose (including subjects who switched from placebo to secukinumab Q4W at Week 16). Adverse events were assessed up to Week 60	Subjects who received at least 1 dose of secukinumab
Total # Affected by any Other Adverse Event	123	125	84	174	174	348
Total # at Risk by any Other Adverse Event	180	180	183	261	266	527
Gastrointestinal disorders						
Abdominal pain	4 (2.22%)	7 (3.89%)	2 (1.09%)	5 (1.92%)	10 (3.76%)	15 (2.85%)
Abdominal pain upper	3 (1.67%)	9 (5.00%)	1 (0.55%)	4 (1.53%)	10 (3.76%)	14 (2.66%)
Constipation	4 (2.22%)	1 (0.56%)	2 (1.09%)	4 (1.53%)	1 (0.38%)	5 (0.95%)
Dental caries	4 (2.22%)	1 (0.56%)	0 (0.00%)	4 (1.53%)	1 (0.38%)	5 (0.95%)
Diarrhoea	13 (7.22%)	14 (7.78%)	13 (7.10%)	19 (7.28%)	19 (7.14%)	38 (7.21%)
Gastrooesophageal reflux disease	4 (2.22%)	4 (2.22%)	1 (0.55%)	7 (2.68%)	6 (2.26%)	13 (2.47%)
Haemorrhoids	1 (0.56%)	5 (2.78%)	0 (0.00%)	1 (0.38%)	5 (1.88%)	6 (1.14%)
Nausea	6 (3.33%)	5 (2.78%)	4 (2.19%)	12 (4.60%)	7 (2.63%)	19 (3.61%)
Toothache	6 (3.33%)	5 (2.78%)	0 (0.00%)	7 (2.68%)	5 (1.88%)	12 (2.28%)

Vomiting	2 (1.11%)	1 (0.56%)	1 (0.55%)	6 (2.30%)	1 (0.38%)	7 (1.33%)
General disorders and administration site conditions						
Fatigue	4 (2.22%)	6 (3.33%)	2 (1.09%)	7 (2.68%)	7 (2.63%)	14 (2.66%)
Influenza like illness	1 (0.56%)	5 (2.78%)	0 (0.00%)	1 (0.38%)	5 (1.88%)	6 (1.14%)
Pyrexia	7 (3.89%)	8 (4.44%)	3 (1.64%)	9 (3.45%)	12 (4.51%)	21 (3.98%)
Infections and infestations						
Bronchitis	5 (2.78%)	5 (2.78%)	2 (1.09%)	5 (1.92%)	7 (2.63%)	12 (2.28%)
Conjunctivitis	4 (2.22%)	6 (3.33%)	0 (0.00%)	4 (1.53%)	7 (2.63%)	11 (2.09%)
COVID-19	10 (5.56%)	7 (3.89%)	3 (1.64%)	13 (4.98%)	14 (5.26%)	27 (5.12%)
Ear infection	4 (2.22%)	1 (0.56%)	0 (0.00%)	5 (1.92%)	1 (0.38%)	6 (1.14%)
Folliculitis	9 (5.00%)	2 (1.11%)	3 (1.64%)	9 (3.45%)	4 (1.50%)	13 (2.47%)
Influenza	5 (2.78%)	1 (0.56%)	0 (0.00%)	7 (2.68%)	1 (0.38%)	8 (1.52%)
Nasopharyngitis	21 (11.67%)	18 (10.00%)	16 (8.74%)	28 (10.73%)	25 (9.40%)	53 (10.06%)
Oral candidiasis	5 (2.78%)	1 (0.56%)	0 (0.00%)	5 (1.92%)	3 (1.13%)	8 (1.52%)
Pharyngitis	3 (1.67%)	6 (3.33%)	3 (1.64%)	4 (1.53%)	9 (3.38%)	13 (2.47%)
Rhinitis	4 (2.22%)	4 (2.22%)	1 (0.55%)	6 (2.30%)	7 (2.63%)	13 (2.47%)
Sinusitis	3 (1.67%)	3 (1.67%)	3 (1.64%)	7 (2.68%)	3 (1.13%)	10 (1.90%)
Skin candida	6 (3.33%)	4 (2.22%)	1 (0.55%)	8 (3.07%)	4 (1.50%)	12 (2.28%)
Sweat gland infection	3 (1.67%)	2 (1.11%)	3 (1.64%)	9 (3.45%)	2 (0.75%)	11 (2.09%)
Tonsillitis	2 (1.11%)	4 (2.22%)	0 (0.00%)	4 (1.53%)	5 (1.88%)	9 (1.71%)
Upper respiratory tract infection	13 (7.22%)	8 (4.44%)	7 (3.83%)	16 (6.13%)	11 (4.14%)	27 (5.12%)
Urinary tract infection	7 (3.89%)	7 (3.89%)	5 (2.73%)	8 (3.07%)	12 (4.51%)	20 (3.80%)
Injury, poisoning and procedural complications						

Ligament sprain	1 (0.56%)	4 (2.22%)	0 (0.00%)	1 (0.38%)	5 (1.88%)	6 (1.14%)
Investigations						
Gamma-glutamyltransferase increased	5 (2.78%)	1 (0.56%)	0 (0.00%)	5 (1.92%)	1 (0.38%)	6 (1.14%)
Lipase increased	3 (1.67%)	7 (3.89%)	1 (0.55%)	5 (1.92%)	7 (2.63%)	12 (2.28%)
SARS-CoV-2 test positive	3 (1.67%)	4 (2.22%)	3 (1.64%)	5 (1.92%)	4 (1.50%)	9 (1.71%)
Weight decreased	0 (0.00%)	4 (2.22%)	0 (0.00%)	0 (0.00%)	4 (1.50%)	4 (0.76%)
Musculoskeletal and connective tissue disorders						
Arthralgia	7 (3.89%)	4 (2.22%)	5 (2.73%)	11 (4.21%)	9 (3.38%)	20 (3.80%)
Back pain	4 (2.22%)	12 (6.67%)	4 (2.19%)	7 (2.68%)	14 (5.26%)	21 (3.98%)
Myalgia	3 (1.67%)	4 (2.22%)	3 (1.64%)	4 (1.53%)	6 (2.26%)	10 (1.90%)
Nervous system disorders						
Dizziness	4 (2.22%)	7 (3.89%)	3 (1.64%)	6 (2.30%)	7 (2.63%)	13 (2.47%)
Headache	31 (17.22%)	27 (15.00%)	16 (8.74%)	39 (14.94%)	36 (13.53%)	75 (14.23%)
Psychiatric disorders						
Depression	6 (3.33%)	5 (2.78%)	4 (2.19%)	6 (2.30%)	5 (1.88%)	11 (2.09%)
Reproductive system and breast disorders						
Dysmenorrhoea	2 (1.11%)	5 (2.78%)	0 (0.00%)	3 (1.15%)	5 (1.88%)	8 (1.52%)
Respiratory, thoracic and mediastinal disorders						
Cough	5 (2.78%)	7 (3.89%)	3 (1.64%)	6 (2.30%)	9 (3.38%)	15 (2.85%)
Oropharyngeal pain	8 (4.44%)	8 (4.44%)	1 (0.55%)	8 (3.07%)	9 (3.38%)	17 (3.23%)
Skin and subcutaneous tissue disorders						

Dermatitis	3 (1.67%)	4 (2.22%)	1 (0.55%)	4 (1.53%)	4 (1.50%)	8 (1.52%)
Eczema	10 (5.56%)	6 (3.33%)	1 (0.55%)	11 (4.21%)	7 (2.63%)	18 (3.42%)
Hidradenitis	21 (11.67%)	23 (12.78%)	14 (7.65%)	26 (9.96%)	31 (11.65%)	57 (10.82%)
Intertrigo	4 (2.22%)	5 (2.78%)	0 (0.00%)	6 (2.30%)	8 (3.01%)	14 (2.66%)
Pruritus	8 (4.44%)	3 (1.67%)	5 (2.73%)	11 (4.21%)	5 (1.88%)	16 (3.04%)
Psoriasis	6 (3.33%)	4 (2.22%)	0 (0.00%)	6 (2.30%)	6 (2.26%)	12 (2.28%)
Vascular disorders						
Hypertension	11 (6.11%)	6 (3.33%)	2 (1.09%)	14 (5.36%)	7 (2.63%)	21 (3.98%)

Other Relevant Findings

none

Conclusion:

The study met the pre-defined primary endpoint (HiSCR50 response) at Week 16 for both secukinumab dose regimens.

The pre-defined secondary endpoints of AN count and NRS30 (skin pain) at Week 16 were met for the secukinumab 300 mg Q2W dose regimen, and the pre-defined secondary endpoints up to Week 16 of AN count and flare were met for the secukinumab 300 mg Q4W dose regimen.

The safety profiles for secukinumab 300 mg Q2W and Q4W were comparable at Week 52 and consistent with the previously safety profile of secukinumab across other approved indications. No new safety signals were observed, and no increased risks were seen with the higher Q2W dosing. Overall rates of AEs, non-fatal SAEs, and discontinuations due to AEs were comparable across treatment groups, with no dose-response effects noted.

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Date of Clinical Trial Report

Dec-26-2022