NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

secukinumab / AIN457

Trial Indication(s)

psoriatic arthritis

Protocol Number

CAIN457F2336

Protocol Title

A phase III, randomized, double-blind, placebo-controlled multicenter study of subcutaneous (sc) secukinumab (150 mg) in pre-filled syringe, with or without loading regimen, to demonstrate efficacy, safety and tolerability up to 2 years in patients with active psoriatic arthritis (FUTURE 4)

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase III

Study Start/End Dates

Study Start Date: May 2015 (Actual)
Primary Completion Date: December 2017 (Actual)
Study Completion Date: December 2017 (Actual)

Reason for Termination (If applicable)

Study Design/Methodology

This multicenter study used a randomized, double-blind, placebo-controlled, parallel-group design. A screening (SCR) period running up to 10 weeks before randomization was used to assess patient eligibility followed by 104 weeks of treatment.

At Baseline (BSL) approximately 318 patients whose eligibility was confirmed were to be randomized to one of three treatment groups (1:1:1). Patients were stratified at randomization on the basis of previous anti-TNF therapy as TNF-naïve or TNF-IR. The only condition thatwas placed on enrollment targets for each stratum was that no less than 65% of patients per arm (69 patients) were TNF-alpha inhibitor naïve (or, no more than 35% of patients were TNF-IR).

At each study treatment visit, one (for secukinumab 150 mg) sc injection in the form of pre-filled syringe (PFS) was administered, since secukinumab is available in 1.0 mL (150 mg) PFS. Placebo to secukinumab was also available in 1.0 mL to match the active drug.

- Group 1 - Secukinumab 150 mg sc without loading regimen:
  Secukinumab 150 mg (1.0 mL PFS of 150 mg dose) administered at BSL, followed by placebo (1.0 mL PFS) at Weeks 1, 2 and 3, followed by secukinumab 150 mg (1.0 mL PFS of150 mg dose) dosing every four weeks starting at Week 4.
- Group 2 - Secukinumab 150 mg sc with loading regimen:
  Secukinumab 150 mg (1.0 mL PFS of 150 mg dose) administered at BSL, Weeks 1, 2 and 3, followed by dosing every four weeks starting at Week 4.
- Group 3 - Placebo sc:
  Placebo (1.0 mL PFS) administered at BSL, Weeks 1, 2 and 3, followed by dosing every four weeks starting at Week 4.

At Week 16, all patients were classified as responders (≥20% improvement from BSL in both tender joint count (TJC) and swollen joint count (SJC)) or non-responders (<20% improvement from BSL in either TJC or SJC) and those who were originally randomized to placebo were re-assigned in the Interactive Response Technology (IRT):

- Patients who were non-responders received secukinumab 150 mg sc (1.0 mL PFS of150 mg dose) without loading regimen every 4 weeks starting at Week 16.
- Patients who were responders continued to receive placebo sc (1.0 mL PFS) every 4 weeks until Week 24.

Starting at Week 24, all patients who continued to receive placebo as responders at Week 16 were re-assigned to receive secukinumab 150 mg sc (1.0 mL PFS of 150 mg dose) without loading regimen every 4 weeks starting at Week 24. Thus, starting at Week 24, patients in all three arms received secukinumab 150 mg in an open-label fashion, since no patients were on placebo starting at Week 24 and all patients received a single injection of 1.0 mL PFS of 150 mg dose. However, original randomized treatment assignment to secukinumab 150 mg Load, secukinumab 150 mg No Load, or placebo remained double-blinded to all patients and investigators/site staff.

After approval and implementation of protocol Amendment 2, at any site visit, the secukinumab dose could be escalated from 150 mg to 300 mg for patients whose signs and symptoms were not well controlled with the current dose of 150 mg, and may improve with higher dose as judged by the investigator. A dose of secukinumab 300 mg was administered as two single subcutaneous (sc) injections of secukinumab 150 mg.

When dose escalation to 300 mg every 4 weeks had been performed for a patient, no dose reduction back to 150 mg every 4 weeks was allowed at a later time for that patient.

After the Week 52 data base lock (DBL) and analyses were completed, site personnel and patients could be unblinded to the original randomized treatment assignment at BSL. The patient continued to receive the same active dose of secukinumab as open-label treatment, unless escalated by investigator, until Week 104 (with last dose at Week 100).

A follow-up visit was to be done 12 weeks after last study treatment administration for all patients, regardless of whether they completed the entire study as planned or discontinue prematurely.

Centers

72 centers in 13 countries: Czech Republic(5), United States(20), Sweden(1), Bulgaria(2), Australia(4), Belgium(5), Italy(5), Canada(4), Germany(10), France(4), Poland(6), United Kingdom(1), Russia(5)

Objectives:

Primary Objective

The primary objective was to demonstrate that the efficacy of secukinumab 150 mg sc, with or without loading regimen, at Week 16 was superior to placebo based on proportion of patients achieving American College of Rheumatology 20 (ACR20) response in patients with active PsA. The primary objective was reported in the CAIN457F2336 PsA Interim analyses at Week 52 CSR dated 14-Jun-2017.

Secondary Objectives

- The improvement on secukinumab 150 mg, with or without loading, at Week 16 is superior to placebo for the disease activity assessed by the changes in Disease Activity Score for 28 joints (DAS28-CRP) (utilizing high sensitivity C-reactive protein [hsCRP]) relative to baseline.
- The efficacy of secukinumab 150 mg, with or without loading, at Week 16 is superior to placebo based on the proportion of patients with at least 3% body surface area (BSA) with psoriasis achieving Psoriasis Area and Severity Index 75 (PASI75) response.
- The improvement on secukinumab 150 mg, with or without loading, at Week 16 is superior to placebo for medical outcome short form health survey physical component summary score (SF-36 PCS) relative to baseline.
- The efficacy of secukinumab 150 mg, with or without loading, at Week 16 is superior to placebo based on the proportion of patients achieving an ACR50 response.
- The efficacy of secukinumab 150 mg, with or without loading, at Week 4 is superior to placebo based on the proportion of patients achieving an ACR20 response.
- Overall safety and tolerability of secukinumab.

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

Secukinumab 75 mg and 150 mg subcutaneous injection using pre-filled syringes

Statistical Methods

Summary statistics for continuous variables included N, mean, standard deviation, minimum, lower quartile, median, upper quartile, maximum. Summary statistics for discrete variables were presented in contingency tables and included absolute and relative frequencies.

If not otherwise specified, p-values and confidence intervals were two-sided.

Unless otherwise stated, the level of significance was set to 5% (two-sided, family-wise type-I-error).

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Diagnosis of Psoriatic Arthritis (PsA) classified by ClASsification criteria for Psoriatic ARthritis (CASPAR) criteria.
- Rheumatoid factor and anti-cyclic citrullinated peptide (CCP) antibodies negative.
- Diagnosis of active plaque psoriasis or nail changes consistent with psoriasis.
- Inadequate control of symptoms with NSAID.

Exclusion Criteria:

- Chest X-ray or chest magnetic resonance imaging (MRI) with evidence of ongoing infectious or malignant process.
- Subjects taking high potency opioid analgesics.
- Previous exposure to secukinumab or other biologic drug directly targeting interleukin-17 (IL-17) or IL-17 receptor.
- Ongoing use of prohibited psoriasis treatments / medications.
- Subjects who have ever received biologic immunomodulating agents except for those targeting TNFα.
- Previous treatment with any cell-depleting therapies.

Participant Flow Table

Overall Study

	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo
Started	114	113	107

Completed	89	88	95
Not Completed	25	25	12
Death	0	0	1
Subject/Guardian Decision	6	3	2
Physician Decision	1	2	1
Lost to Follow-up	1	0	0
Lack of Efficacy	11	12	6
Adverse Event	6	8	2

Baseline Characteristics

	Secukinumab 150 mg	**Secukinumab 150 mg No load**	**Placebo**	**Total**
Number of Participants [units: participants]	114	113	107	334
Age Continuous (units: Years) Mean ± Standard Deviation				
	48.3±12.17	50.4±11.78	48.5±12.12	49.0±12.03
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)				
Female	47	51	43	141
Male	67	62	64	193
Race/Ethnicity, Customized (units: Participants)				

Asian	1	0	0	1
White	113	113	107	333

Summary of Efficacy

Primary Outcome Result(s)

Number of participants with American College of Rheumatology 20 (ACR20) response at week 16

	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo
Number of Participants Analyzed [units: participants]	114	113	107
Number of participants with American College of Rheumatology 20 (ACR20) response at week 16 (units: Participants)			
	47	45	21

Secondary Outcome Result(s)

Disease Activity Score (DAS-C28-CRP) score change from baseline using MMRM at week 16

	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo

Number of Participants Analyzed [units: participants]	114	113	107
Disease Activity Score (DAS-C28-CRP) score change from baseline using MMRM at week 16 (units: scores) Least Squares Mean ± Standard Error			
	-0.98 ± 0.106	-0.84 ± 0.106	-0.21 ± 0.107

Psoriatic Area and Severity Index 75 (PASI75) at week 16

	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo
Number of Participants Analyzed [units: participants]	55	54	62
Psoriatic Area and Severity Index 75 (PASI75) at week16 (units: participants)			
	29	27	5

Short Form Health Survey Physical Component Score (SF-36-PCS) at week 16

	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo non-responder
Number of Participants Analyzed [units: participants]	114	113	77
Short Form Health			

Survey Physical Component Score (SF-36-PCS) at week 16 (units: scores) Least Squares Mean ± Standard Error			
	3.42 ± 0.5676	3.44 ± 0.5678	0.63 ± 0.586

Number of participants with American College of Rheumatology 50 (ACR50) at week 16

	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo
Number of Participants Analyzed [units: participants]	114	113	114
Number of participants with American College of Rheumatology 50 (ACR50) at week 16 (units: participants)			
	26	19	7

Number of participants with American College of Rheumatology 20 (ACR20) response at week 4

	Secukinumab 150 mg	Secukinumab 150 mg No load	Placebo
Number of Participants Analyzed [units: participants]	114	113	114
Number of participants with American College of Rheumatology 20 (ACR20) response at			

week 4
(units: participants)

	33	26	22

Summary of Safety

Safety Results

All-Cause Mortality

	Any AIN457 150 mg N = 334	Any AIN457 300 mg N = 136	Any AIN457 N = 334	Placebo N = 114
Total participants affected	1 (0.30%)	1 (0.74%)	2 (0.60%)	0 (0.00%)

Serious Adverse Events by Preferred Term and System Organ Class

Time Frame	Adverse Events (AEs) are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All AEs reported in this record are from date of First Patient First Treatment until Last Patient Last Visit up to approximately 104 weeks
Additional Description	Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events fields "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.
Source Vocabulary for Table Default	MedDRA (20.1)
Assessment Type for Table Default	Systematic Assessment

	Any AIN457 150 mg N = 334	Any AIN457 300 mg N = 136	Any AIN457 N = 334	Placebo N = 114
Total participants affected	47 (14.07%)	12 (8.82%)	59 (17.66%)	5 (4.39%)
Cardiac disorders				
Acute myocardial infarction	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Coronary artery disease	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Myocardial infarction	2 (0.60%)	0 (0.00%)	2 (0.60%)	0 (0.00%)
Myocardial ischaemia	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Endocrine disorders				
Goitre	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Gastrointestinal disorders				
Abdominal hernia	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Colitis ulcerative	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)
Crohn's disease	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Inguinal hernia	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Pancreatitis acute	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.88%)
General disorders and administration site conditions				
Non-cardiac chest pain	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)
Hepatobiliary disorders				
Biliary colic	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)

Cholelithiasis	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)
Drug-induced liver injury	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Hepatitis alcoholic	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Immune system disorders				
Immunosuppression	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)
Infections and infestations				
Atypical pneumonia	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)
Bacterial pyelonephritis	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Campylobacter gastroenteritis	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Erysipelas	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Escherichia urinary tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.88%)
Gastroenteritis	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Hepatitis A	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Influenza	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Pilonidal cyst	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.88%)
Pyelonephritis	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)
Sepsis	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Urinary tract infection	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Urosepsis	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Viral upper respiratory tract infection	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Injury, poisoning and procedural complications				
Fall	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)

Joint dislocation	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Laceration	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Post procedural haemorrhage	1 (0.30%)	1 (0.74%)	2 (0.60%)	0 (0.00%)
Rib fracture	2 (0.60%)	0 (0.00%)	2 (0.60%)	0 (0.00%)
Tendon rupture	1 (0.30%)	1 (0.74%)	2 (0.60%)	0 (0.00%)
Thermal burn	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Tibia fracture	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Upper limb fracture	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Investigations				
Alanine aminotransferase increased	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Aspartate aminotransferase increased	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Metabolism and nutrition disorders				
Hyponatraemia	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Musculoskeletal and connective tissue disorders				
Arthralgia	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Arthritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.88%)
Cervical spinal stenosis	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Intervertebral disc protrusion	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Joint range of motion decreased	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)

Loose body in joint	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Musculoskeletal chest pain	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Osteoarthritis	3 (0.90%)	0 (0.00%)	3 (0.90%)	0 (0.00%)
Polyarthritis	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Psoriatic arthropathy	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Rotator cuff syndrome	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Adrenal adenoma	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)
Breast cancer	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Chronic lymphocytic leukaemia	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Fibroma	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Malignant melanoma	1 (0.30%)	1 (0.74%)	2 (0.60%)	0 (0.00%)
Papillary thyroid cancer	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Parathyroid tumour benign	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Prostate cancer	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Squamous cell carcinoma	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Undifferentiated sarcoma	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Uterine leiomyoma	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)
Nervous system disorders				
Balance disorder	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Cerebrovascular	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)

accident				
Cervicogenic headache	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.88%)
Facial paralysis	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Syncope	2 (0.60%)	0 (0.00%)	2 (0.60%)	0 (0.00%)
Product issues				
Device dislocation	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Device fastener issue	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Psychiatric disorders				
Disorientation	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Renal and urinary disorders				
Nephrolithiasis	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Ureteric compression	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)
Reproductive system and breast disorders				
Adenomyosis	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)
Interstitial lung disease	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)
Nasal turbinate hypertrophy	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Pleural effusion	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Pneumothorax	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Skin and subcutaneous tissue disorders				
Skin ulcer	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)

Vascular disorders				
Hypertensive crisis	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Peripheral arterial occlusive disease	0 (0.00%)	1 (0.74%)	1 (0.30%)	0 (0.00%)
Raynaud's phenomenon	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Thrombophlebitis	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)
Varicose vein	1 (0.30%)	0 (0.00%)	1 (0.30%)	0 (0.00%)

Other Adverse Events by Preferred Term and System Organ Class

Time Frame	Adverse Events (AEs) are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All AEs reported in this record are from date of First Patient First Treatment until Last Patient Last Visit up to approximately 104 weeks
Additional Description	Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events fields "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.
Source Vocabulary for Table Default	MedDRA (20.1)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	2%

	Any AIN457 150 mg N = 334	**Any AIN457 300 mg N = 136**	**Any AIN457 N = 334**	**Placebo N = 114**
Total participants affected	252 (75.45%)	89 (65.44%)	267 (79.94%)	61 (53.51%)
Blood and lymphatic system disorders				
Leukopenia	9 (2.69%)	3 (2.21%)	12 (3.59%)	0 (0.00%)

Cardiac disorders				
Ventricular extrasystoles	3 (0.90%)	3 (2.21%)	6 (1.80%)	0 (0.00%)
Ear and labyrinth disorders				
Vertigo	8 (2.40%)	1 (0.74%)	9 (2.69%)	1 (0.88%)
Gastrointestinal disorders				
Abdominal pain	10 (2.99%)	1 (0.74%)	11 (3.29%)	1 (0.88%)
Diarrhoea	29 (8.68%)	4 (2.94%)	32 (9.58%)	3 (2.63%)
Dyspepsia	6 (1.80%)	3 (2.21%)	9 (2.69%)	0 (0.00%)
Nausea	19 (5.69%)	2 (1.47%)	21 (6.29%)	6 (5.26%)
Toothache	3 (0.90%)	3 (2.21%)	5 (1.50%)	0 (0.00%)
Vomiting	8 (2.40%)	2 (1.47%)	10 (2.99%)	1 (0.88%)
General disorders and administration site conditions				
Fatigue	13 (3.89%)	3 (2.21%)	16 (4.79%)	2 (1.75%)
Oedema peripheral	5 (1.50%)	2 (1.47%)	7 (2.10%)	1 (0.88%)
Pyrexia	11 (3.29%)	1 (0.74%)	12 (3.59%)	1 (0.88%)
Hepatobiliary disorders				
Hepatic steatosis	6 (1.80%)	2 (1.47%)	8 (2.40%)	0 (0.00%)
Infections and infestations				
Bronchitis	31 (9.28%)	8 (5.88%)	38 (11.38%)	2 (1.75%)
Cystitis	7 (2.10%)	3 (2.21%)	10 (2.99%)	1 (0.88%)
Furuncle	6 (1.80%)	1 (0.74%)	7 (2.10%)	0 (0.00%)
Gastroenteritis	15 (4.49%)	5 (3.68%)	19 (5.69%)	3 (2.63%)

Gastroenteritis viral	7 (2.10%)	1 (0.74%)	8 (2.40%)	1 (0.88%)
Gingivitis	6 (1.80%)	1 (0.74%)	7 (2.10%)	2 (1.75%)
Influenza	11 (3.29%)	4 (2.94%)	14 (4.19%)	2 (1.75%)
Laryngitis	5 (1.50%)	3 (2.21%)	8 (2.40%)	1 (0.88%)
Nasopharyngitis	86 (25.75%)	21 (15.44%)	96 (28.74%)	16 (14.04%)
Oral herpes	11 (3.29%)	4 (2.94%)	13 (3.89%)	3 (2.63%)
Pharyngitis	23 (6.89%)	4 (2.94%)	25 (7.49%)	1 (0.88%)
Pulpitis dental	8 (2.40%)	2 (1.47%)	10 (2.99%)	0 (0.00%)
Respiratory tract infection	10 (2.99%)	2 (1.47%)	11 (3.29%)	2 (1.75%)
Rhinitis	9 (2.69%)	5 (3.68%)	14 (4.19%)	1 (0.88%)
Sinusitis	29 (8.68%)	11 (8.09%)	34 (10.18%)	1 (0.88%)
Tonsillitis	10 (2.99%)	6 (4.41%)	14 (4.19%)	0 (0.00%)
Upper respiratory tract infection	48 (14.37%)	11 (8.09%)	55 (16.47%)	6 (5.26%)
Urinary tract infection	17 (5.09%)	1 (0.74%)	18 (5.39%)	4 (3.51%)
Viral infection	6 (1.80%)	2 (1.47%)	8 (2.40%)	1 (0.88%)
Viral upper respiratory tract infection	11 (3.29%)	2 (1.47%)	13 (3.89%)	1 (0.88%)
Injury, poisoning and procedural complications				
Contusion	10 (2.99%)	1 (0.74%)	11 (3.29%)	1 (0.88%)
Fall	11 (3.29%)	2 (1.47%)	13 (3.89%)	1 (0.88%)
Limb injury	10 (2.99%)	1 (0.74%)	11 (3.29%)	0 (0.00%)
Investigations				
Alanine aminotransferase	7 (2.10%)	1 (0.74%)	8 (2.40%)	1 (0.88%)

increased				
Hepatic enzyme increased	6 (1.80%)	2 (1.47%)	8 (2.40%)	0 (0.00%)
Weight increased	6 (1.80%)	1 (0.74%)	7 (2.10%)	1 (0.88%)
Metabolism and nutrition disorders				
Dyslipidaemia	9 (2.69%)	1 (0.74%)	9 (2.69%)	4 (3.51%)
Hypercholesterolaemia	13 (3.89%)	4 (2.94%)	17 (5.09%)	1 (0.88%)
Hyperlipidaemia	5 (1.50%)	2 (1.47%)	7 (2.10%)	0 (0.00%)
Vitamin D deficiency	6 (1.80%)	1 (0.74%)	7 (2.10%)	0 (0.00%)
Musculoskeletal and connective tissue disorders				
Arthralgia	11 (3.29%)	4 (2.94%)	15 (4.49%)	1 (0.88%)
Back pain	14 (4.19%)	2 (1.47%)	15 (4.49%)	2 (1.75%)
Osteoarthritis	7 (2.10%)	2 (1.47%)	9 (2.69%)	0 (0.00%)
Pain in extremity	6 (1.80%)	1 (0.74%)	7 (2.10%)	1 (0.88%)
Psoriatic arthropathy	21 (6.29%)	12 (8.82%)	28 (8.38%)	5 (4.39%)
Rotator cuff syndrome	5 (1.50%)	2 (1.47%)	7 (2.10%)	0 (0.00%)
Spinal pain	6 (1.80%)	1 (0.74%)	7 (2.10%)	0 (0.00%)
Temporomandibular joint syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (2.63%)
Nervous system disorders				
Dizziness	5 (1.50%)	0 (0.00%)	5 (1.50%)	3 (2.63%)
Headache	25 (7.49%)	5 (3.68%)	30 (8.98%)	10 (8.77%)
Migraine	6 (1.80%)	1 (0.74%)	7 (2.10%)	0 (0.00%)
Respiratory, thoracic and mediastinal				

disorders				
Cough	16 (4.79%)	0 (0.00%)	16 (4.79%)	2 (1.75%)
Oropharyngeal pain	13 (3.89%)	3 (2.21%)	16 (4.79%)	1 (0.88%)
Skin and subcutaneous tissue disorders				
Eczema	7 (2.10%)	0 (0.00%)	7 (2.10%)	2 (1.75%)
Pruritus	6 (1.80%)	2 (1.47%)	8 (2.40%)	1 (0.88%)
Psoriasis	7 (2.10%)	5 (3.68%)	12 (3.59%)	1 (0.88%)
Rash	6 (1.80%)	2 (1.47%)	8 (2.40%)	0 (0.00%)
Vascular disorders				
Hypertension	28 (8.38%)	2 (1.47%)	30 (8.98%)	4 (3.51%)

Other Relevant Findings

NA

Conclusion:

The purpose of this Week 104 final report for study CAIN457F2336 was to provide long-term efficacy, safety and tolerability data, up to 2 years, for secukinumab in the treatment of PsA and investigate the efficacy after secukinumab dose escalation from 150 mg to 300 mg in the subgroup of patients whose secukinumab dose was escalated.

The study population consisted of 341 patients who were originally randomized to 3 treatment groups: secukinumab 150 mg sc load (n=114), secukinumab 150 mg sc no load (n=113) and placebo (n=114). The groups were generally well balanced with respect to demographics, disease history, and baseline characteristics. Approximately one-quarter of patients had a history or inadequate response to a TNF-alpha inhibitor at study entry.

This study achieved the primary endpoint. Both secukinumab treatment regimens (150 mg sc load and 150 mg sc no load) demonstrated a highly superior ACR20 response compared to placebo at Week 16 using non-responder imputation. At this ACR response level, no difference was observed between the load and no-load secukinumab dose regimens either immediately after loading at Week 4 (last hierarchical secondary endpoint) or later at Week 16. All secondary endpoints (except for ACR20 at Week 4) were also met by both secukinumab treatment regimens (150 mg sc load and 150 mg sc no load) which were superior to placebo for DAS28-CRP, PASI75, SF-36 PCS and ACR50 responses at Week 16.

The study showed no new or unexpected safety signals from what is currently known. Overall, there were no clinically meaningful differences in the safety profile between the secukinumab dose regimens 150 mg load, 150 mg no load and 300 mg during the entire 104-week treatment period. The most commonly reported treatment-emergent AEs by primary SOC in the Any-secukinumab treatment group were infections and infestations (236 patients, 70.7%), musculoskeletal and connective tissue disorders (110 patients, 32.9%), gastrointestinal disorders (109 patients, 32.6%), skin and subcutaneous tissue disorders (73 patients, 21.9%) and nervous system disorders (67 patients, 20.1%)

Date of Clinical Trial Report

6 June 2018