Sponsor

Novartis

Generic Drug Name

Secukinumab

Therapeutic Area of Trial

Ankylosing spondylitis (AS)

Protocol Number

CAIN457A2209E1

Title

An open-label non-randomized extension study to evaluate the safety and tolerability of IN457 (anti interleukin-17 monoclonal antibody) in patients with moderate to severe ankylosing spondylitis.

Study Phase

II

Study Start/End Dates

14 Apr 2010 to 05 Dec 2012

Study Design/Methodology

Multicenter, open-label, non-randomized trial without comparator with active treatment over 24 weeks initially (Part 1) with a possible extension of a further 6 months (Part 2) for those patients who participated in the core CAIN457A2206 study. Patients received 3 mg/kg secukinumab every 4 weeks, over a period of 52 weeks.

Centers

15 centers in 4 countries: Germany (4), Netherlands (1), United Kingdom (1) and United States (9)

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

Intravenous infusion of 3 mg/kg secukinumab every 4 weeks, over a period of 52 weeks.

Statistical Methods

Categorical variables were summarized by frequency tables. Continuous variables were summarized by descriptive statistics.

All patients who received at least one dose of study drug were included in the safety and tolerability evaluation.

All completed patients with quantifiable PK measurements and no major protocol deviations with impact on PK data were included in the PK analysis set.

All patients with a least one evaluable post-treatment pharmacodynamic (PD) measurements and no major protocol deviations with impact on PD data were included in the PD analysis set.

All data for background and demographic variables were listed by patient. Summary statistics were provided.

Relevant medical history, current medical conditions, results of laboratory screens and any other relevant information were listed by patient.

Drug administration records and any concomitant medication used were listed by treatment and patient.

Safety results were presented based on the treatment group patients were enrolled in the previous core study.

- Secukinumab 2x10 mg/kg
- Secukinumab 2x1.0 mg/kg
- Secukinumab 2x0.1 mg/kg
- Placebo

All vital signs data were listed by patient and visit/time, and if ranges were available abnormalities (and relevant orthostatic changes) were flagged. Summary statistics were provided by visit/time.

All ECG data were listed by patient and visit/time, abnormalities were flagged. Summary statistics were provided by visit/time.

All laboratory data were listed by patient and visit/time and abnormalities were flagged. Summary statistics were provided by visit/time.

All information obtained on adverse events was displayed by patient.

The number and percentage of patients with adverse events was counted by body system and preferred term. A patient with multiple adverse events within a body system was only counted once towards the total of this body system.

Concomitant medications were also listed by patient.

No formal statistical hypotheses of the safety or tolerability were tested for this study.

No statistical analysis of immunogenicity data was done.

For PK analyses, descriptive statistics of concentration over time for the extension phase (e.g. N, minimum, maximum, artithmetic and geometric mean, standard deviation, median and range) were presented.

The PD variables were summarized across the core and extension studies by treatment and over time. Mean plots and individual profiles over time were presented for selected parameters. No inferential analyses of these data were planned. Individual data listing were present only for baseline values from the core study and all data from the extension study.

Study Population: Inclusion/Exclusion Criteria and Demographics

Inclusion criteria

- Patients who participated and completed the core CAIN457A2209 study up to and including the end of study (EoS) i.e. Visit 17 (Week 28), could have entered the extension study upon signing the informed consent.
- Patients who discontinued the core study due to unsatisfactory therapeutic effect at their Visit 14 (Week 16) or later could enter the extension study within 3 weeks of completing the study discontinuation visit of the core study, provided that at their discontinuation visit they fulfilled either one of the criteria below. Patients who did not enter the extension study within 3 weeks of completing the study discontinuation visit of the core study, were required to come for an additional baseline visit (Visit 17) and were required to fulfill either one of the criteria below:
    - No improvement (compared with the core study baseline) in two out of the following four domains: patient global assessment, pain, Bath Ankylosing Spondylitis Functional Index (BASFI) and the mean of the two morning stiffness questions from the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Or
    - Deterioration (compared with the core study baseline) in one of the four domains (deterioration defined as >=20% worsening and an absolute worsening of >=1 unit)

Exclusion criteria

- Patients for whom continued treatment with AIN457 was not considered appropriate by the treating physician.
- Patients who were non-compliant or who demonstrated a major protocol violation in the core CAIN457A2209 study.

- Patients who discontinued from the core CAIN457A2209 study before Visit 14 (Week 16).
- Pregnant or lactating women
- Presence of active infection
- Positive purified protein derivative (PPD) or HIV test in patients where repeated testing was deemed appropriate due to their risk profile

Participant Flow

Patient disposition – n (%) of patients (all patients)

	Dose Group-(1) N=21	Dose Group-(2) N=8	Dose Group-(3) N=7	Placebo/ Secukinumab N=3	Total N=39
Patients					
Completed	13 (61.9)	6 (75.0)	6 (85.7)	3 (100.0)	28 (71.8)
Discontinued	8 (38.1)	2 (25.0)	1 (14.3)	0	11 (28.2)
Administrative problems	2 (9.5)	0	0	0	2 (5.1)
Serious Adverse Event	2 (9.5)	1 (12.5)	0	0	3 (7.7)
Lost to follow-up	1 (4.8)	0	0	0	1 (2.6)
Patient withdrew consent	1 (4.8)	1 (12.5)	0	0	2 (5.1)
Unsatisfactory therapeutic effect	2 (9.5)	0	1 (14.3)	0	3 (7.7)

Treatment received in core study: (1) Secukinumab 2x10mg/kg, (2) Secukinumab 2x1.0mg/kg, (3) Secukinumab 2x0.1mg/kg

Baseline Characteristics

Demographic summary (all patients)

		Dose Group-(1) N=21	Dose Group-(2) N=8	Dose Group-(3) N=7	Placebo / Secukinumab N=3	Total N=39
Age (years)	Mean (SD)	39.5 (7.56)	47.9 (11.27)	45.9 (8.61)	41.7 (11.59)	42.5 (9.25)
	Median	40.0	46.0	46.0	36.0	41.0
	Range	26 – 52	33 - 64	35 - 63	34 - 55	26 - 64
Gender - n(%)	Male	11 (52)	4 (50)	5 (71)	3 (100)	23 (59)
	Female	10 (48)	4 (50)	2 (29)		16 (41)
Predominant race - n(%)	Caucasian	18 (86)	8 (100)	6 (86)	3 (100)	35 (90)
	Other	2 (10)	0	1 (14)	0	3 (8)
	Black	1 (5)	0		0	1 (3)
Height (cm)	Mean (SD)	170.4 (8.16)	173.8 (7.40)	175.0 (7.02)	179.3 (5.13)	172.6 (7.86)
	Median	169.0	170.5	176.0	178.0	171.0
	Range	153 – 185	167 - 186	164 - 185	175 - 185	153 - 186
Weight (kg)	Mean (SD)	82.2 (19.33)	86.5 (14.64)	77.0 (18.22)	73.3 (21.03)	81.5 (18.07)

		Dose Group-(1) N=21	Dose Group-(2) N=8	Dose Group-(3) N=7	Placebo / Secukinumab N=3	Total N=39
	Median	77.0	83.5	73.0	72.0	77.2
	Range	51 – 123	66 - 114	58 - 105	53 - 95	51 - 123
BMI (kg/m^2)	Mean (SD)	28.2 (6.22)	28.7 (5.32)	24.9 (4.45)	23.0 (7.26)	27.3 (5.90)
	Median	26.1	28.1	24.2	23.5	26.6
	Range	18 – 43	23 - 41	19 - 31	15 - 30	15 - 43

Treatment received in core study: (1) secukinumab 2x10mg/kg, (2) secukinumab 2x1.0mg/kg, (3) secukinumab 2x0.1mg/kg

Outcome measures

Primary Outcome Result(s)

Safety and tolerability: See Safety Results Section.

Secondary Outcome Result(s)

Immunogenicity of secukinumab:

Immunogenicity: Anti-AIN457 antibody
All subjects

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x0.1mg/kg; Ext: AIN457 3mg/kg	One Pt	EXT SCR	-14	10MAR201	14:30	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK0	1	24MAR201	10:50	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	57	19MAY201	10:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	08SEP201	11:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	454	19JUN201	09:55	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-8	05JAN201	10:55	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	13JAN201	09:25	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	54	07MAR201	10:12	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	166	27JUN201	09:20	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	278	17OCT201	10:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	454	10APR201	14:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	EXT SCR	-21	15MAR201	13:40	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK8	57	31MAY201	12:50	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	168	19SEP201	10:42	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x0.1mg/kg; Ext: AIN457 3mg/kg		EWEEK40	281	10JAN201	09:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	449	26JUN201	12:25	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-7	12MAY201	15:12	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK8	57	14JUL201	13:42	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	03NOV201	12:27	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	428	19JUL201	11:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-7	16FEB201	08:20	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	23FEB201	08:11	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	EXT SCR	-16	01MAR201	08:55	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK0	1	17MAR201	08:30	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK8	57	12MAY201	08:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	01SEP201	08:18	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	281	22DEC201	08:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	449	07JUN201	08:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x0.1mg/kg; Ext: AIN457 3mg/kg	One Pt	CEOS/BAS Ext	-18	17FEB201	07:25	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	07MAR201	09:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	57	02MAY201	08:20	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	22AUG201	09:20	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	281	12DEC201	09:05	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	450	29MAY201	08:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
Core: AIN457 2x1.0mg/kg; Ext: AIN457 3mg/kg	One Pt	CEOS/BAS Ext	-18	01NOV201	09:25	No immunogenicity	No inhibition of immunogenicity signal	Early termination
		EWEEK0	1	19NOV201	10:20	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	54	11JAN201	09:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	166	03MAY201	08:55	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	278	23AUG201	09:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	453	14FEB201	10:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x1.0mg/kg; Ext: AIN457 3mg/kg	One Pt	CEOS/BAS Ext	-5	30MAR201	14:15	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	04APR201	10:30	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	57	30MAY201	10:40	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	204	24OCT201	10:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-13	02MAR201	10:41	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	15MAR201	11:42	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	183	13SEP201	12:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	275	14DEC201	10:53	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	422	09MAY201	10:34	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	EWEEK0	1	18MAY201	08:10	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK8	58	14JUL201	08:06	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	174	07NOV201	08:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	282	23FEB201	08:22	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	421	11JUL201	08:25	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x1.0mg/kg; Ext: AIN457 3mg/kg	One Pt	CEOS/BAS Ext	-14	11JAN201	13:00	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	25JAN201	09:50	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	57	22MAR201	09:25	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	R			No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	12JUL201	10:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	283	03NOV201	11:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	449	17APR201	11:30	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	1	10MAY201	10:35	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK8	58	06JUL201	10:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	161	17OCT201	09:55	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	197	22NOV201	11:30	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-21	03MAR201	08:05	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK8	57	19MAY201	08:13	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	08SEP201	08:15	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x1.0mg/kg; Ext: AIN457 3mg/kg		EWEEK40	281	29DEC201	08:15	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	449	14JUN201	08:55	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	EWEEK8	55	16MAY201	10:15	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	171	09SEP201	09:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	281	28DEC201	09:15	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	449	13JUN201	09:05	No immunogenicity	Possible inhibition of immunogenicity signal	NA
Core: AIN457 2x10mg/kg; Ext: AIN457 3mg/kg	One Pt	EXT SCR	-11	07MAY201	10:45	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK0	1	18MAY201	09:50	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK8	57	13JUL201	10:30	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	02NOV201	10:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	281	22FEB201	10:20	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	422	13JUL201	11:40	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x10mg/kg; Ext: AIN457 3mg/kg	One Pt	EXT SCR	-14	06MAY201	13:40	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK0	1	20MAY201	11:55	No immunogenicity	No inhibition of immunogenicity signal	NA
		EEOS	28	16JUN201	11:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	EXT SCR	-18	10MAY201	11:05	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK0	1	28MAY201	11:05	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK8	54	20JUL201	10:15	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	278	01MAR201	10:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	425	26JUL201	11:05	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	EXT SCR	-7	12MAY201	08:50	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK0	1	19MAY201	10:12	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	57	14JUL201	10:40	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	03NOV201	10:25	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	281	23FEB201	10:25	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	412	04JUL201	10:40	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x10mg/kg; Ext: AIN457 3mg/kg	One Pt	EXT SCR	-7	31MAY201	10:30	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK0	1	07JUN201	10:30	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	57	02AUG201	10:20	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	170	23NOV201	10:20	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	431	11AUG201	11:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-13	27JUL201	13:00	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	09AUG201	09:50	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	57	04OCT201	10:15	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	24JAN201	10:15	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	281	16MAY201	10:55	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	456	07NOV201	12:40	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-18	02SEP201	13:15	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	20SEP201	10:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	60	18NOV201	09:25	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x10mg/kg; Ext: AIN457 3mg/kg		EWEEK24	171	09MAR201	10:20	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	340	25AUG201	12:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-15	26OCT201	12:10	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	10NOV201	11:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	57	05JAN201	11:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	27APR201	11:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	281	17AUG201	10:55	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	457	09FEB201	11:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-14	17JAN201	11:25	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	31JAN201	10:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	59	30MAR201	10:20	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	18JUL201	10:30	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	241	28SEP201	13:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	EXT SCR	-7	25MAY201	14:15	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x10mg/kg; Ext: AIN457 3mg/kg		EWEEK0	1	01JUN201	10:30	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	52	22JUL201	09:40	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	16NOV201	09:40	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	281	08MAR201	09:25	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	459	02SEP201	14:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-21	05JUL201	10:15	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	26JUL201	09:50	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	58	21SEP201	12:03	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	10JAN201	10:30	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	200	10FEB201	12:20	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	EXT SCR	-6	25AUG201	15:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK0	1	31AUG201	11:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	57	26OCT201	11:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	171	17FEB201	10:40	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x10mg/kg; Ext: AIN457 3mg/kg		EWEEK40	283	09JUN201	10:25	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	456	29NOV201	13:27	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-16	21SEP201	11:30	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	07OCT201	10:55	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	57	02DEC201	11:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	167	22MAR201	09:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	280	13JUL201	09:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	453	02JAN201	12:25	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-9	28SEP201	12:35	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	07OCT201	11:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	58	03DEC201	10:25	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	168	23MAR201	10:16	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	280	13JUL201	08:55	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	453	02JAN201	14:55	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x10mg/kg; Ext: AIN457 3mg/kg	One Pt	CEOS/BAS Ext	-22	26JAN201	10:24	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	17FEB201	10:40	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	04AUG201	09:56	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	279	22NOV201	11:37	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	454	15MAY201	10:26	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-1	02NOV201	08:15	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	03NOV201	09:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	57	29DEC201	08:40	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	170	21APR201	08:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	296	25AUG201	08:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-2	25OCT201	11:40	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	27OCT201	09:15	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	58	23DEC201	09:50	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	13APR201	11:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x10mg/kg; Ext: AIN457 3mg/kg		EWEEK40	280	02AUG201	10:30	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	R			No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-1	27OCT201	10:20	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	28OCT201	10:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	56	22DEC201	10:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	183	28APR201	11:15	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	294	17AUG201	11:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	EXT SCR	-21	24AUG201	09:40	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK0	1	14SEP201	10:15	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK8	57	09NOV201	11:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	29FEB201	10:30	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	281	20JUN201	10:25	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	449	05DEC201	10:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	EWEEK8	57	28APR201	09:05	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: AIN457 2x10mg/kg; Ext: AIN457 3mg/kg		EWEEK24	169	18AUG201	09:20	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	281	08DEC201	10:00	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	449	24MAY201	08:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	R			No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EXT SCR	-6	07JUN201	09:55	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK0	1	13JUN201	11:00	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK8	59	10AUG201	10:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	170	29NOV201	10:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	277	15MAR201	11:54	No immunogenicity	Possible inhibition of immunogenicity signal	NA
Core: Placebo; Ext: AIN457 3mg/kg	One Pt	CEOS/BAS Ext	-28	05OCT201	10:20	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	02NOV201	09:50	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK8	56	27DEC201	09:40	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal	Comment
Core: Placebo; Ext: AIN457 3mg/kg		EWEEK24	170	20APR201	10:10	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	282	10AUG201	10:40	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	451	26JAN201	11:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	EXT SCR	-13	26MAY201	09:30	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK0	1	08JUN201	10:45	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK8	57	03AUG201	10:50	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	169	23NOV201	10:15	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	283	17MAR201	10:05	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EEOS	449	30AUG201	10:36	No immunogenicity	Possible inhibition of immunogenicity signal	NA
	One Pt	CEOS/BAS Ext	-13	14APR201	14:52	No immunogenicity	No inhibition of immunogenicity signal	
		EWEEK0	1	27APR201	08:25	No immunogenicity	No inhibition of immunogenicity signal	NA
		EWEEK8	56	21JUN201	08:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK24	168	11OCT201	08:40	No immunogenicity	Possible inhibition of immunogenicity signal	NA
		EWEEK40	287	07FEB201	08:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA

Treatment group	Center/ Subject	Visit	Study Day	Sample date	Sample time	Immunogenicity	Inhibition of signal		Comment
Core: Placebo; Ext: AIN457 3mg/kg		EEOS	450	20JUL201	14:35	No immunogenicity	Possible inhibition of immunogenicity signal	NA	

Center and Subject Number removed from table to protect personal data. Replaced with “One Pt”.

Pharmacokinetics of secukinumab at steady state:

Mean secukinumab serum concentrations

Week	N	Mean (SD) (µg/mL)	N	Mean (SD) (µg/mL)	N	Mean (SD) (µg/mL)	N	Mean (SD) (µg/mL)
	Dose Group-(1)		Dose Group-(2)		Dose Group-(3)		Placebo/Secukinumab	
0/pre-inf	21	4.73 (10.1)	7	15.0 (38.4)	5	0.043 (0.059)	3	27.1 (46.9)
0/post-inf	19	64.2 (13.5)	7	58.1 (30.5)	5	56.1 (24.1)	3	63.0 (14.6)
8/pre-inf	19	28.4 (24.3)	8	21.7 (4.20)	5	28.9 (9.31)	3	19.4 (10.7)
8 /post-inf	18	101 (61.4)	8	88.0 (19.2)	6	76.9 (21.7)	3	52.4 (16.0)
16/pre-inf	18	35.7 (34.7)	8	35.8 (20.7)	6	39.6 (25.8)	2	14.6 (8.78)
16/post-inf	17	96.6 (23.1)	8	81.8 (30.2)	6	81.1 (27.5)	2	59.0 (18.5)
20/pre-inf	19	24.9 (15.8)	7	42.1 (26.5)	6	32.6 (6.41)	3	27.2 (15.2)
20/post-inf	19	93.3 (26.2)	7	108 (23.5)	6	104 (22.1)	3	83.2 (38.5)
24/pre-inf	18	27.1 (12.4)	4	24.1 (10.9)	6	37.6 (8.74)	3	25.7 (16.5)
24/post-inf	17	99.0 (20.1)	4	101 (35.0)	6	100 (19.7)	3	83.5 (28.4)
28/pre-inf	16	40.1 (34.6)	4	28.8 (8.98)	6	33.8 (5.91)	2	18.0 (15.4)
28/post-inf	16	99.8 (22.7)	4	82.7 (12.3)	5	92.4 (12.2)	2	71.8 (14.9)
32/pre-inf	14	32.0 (19.6)	4	31.7 (3.33)	5	28.0 (9.69)	3	27.7 (18.2)
32/post-inf	14	90.0 (38.7)	4	128 (39.4)	4	83.6 (20.3)	3	92.5 (9.21)
36/pre-inf	10	41.0 (40.7)	5	26.5 (12.6)	6	34.3 (15.0)	2	26.5 (25.2)
36 /post-inf	10	110 (33.6)	5	99.7 (20.0)	6	107 (30.2)	2	80.2 (35.1)
40/pre-inf	13	26.4 (12.2)	5	27.3 (7.16)	5	33.7 (7.21)	2	13.8 (4.38)
40/post-inf	13	107 (36.4)	4	97.0 (18.5)	5	104 (32.4)	2	74.8 (6.22)
56	12	33.8 (9.62)	5	35.1 (7.62)	6	38.8 (10.3)	3	36.2 (16.9)
64	7	10.5 (3.03)	6	10.6 (3.82)	5	11.3 (4.81)	3	17.1 (10.9)

Treatment received in core study: (1) secukinumab 2x10mg/kg, (2) secukinumab 2x1.0mg/kg, (3) secukinumab 2x0.1mg/kg

Inf: infusion (pre/post)

Total IL-17 concentration in blood at steady state:

Total serum IL-17A was not measured due to assay limitations.

Safety Results

Adverse Events by System Organ Class

	Dose Group-(1) N=21 n (%)	Dose Group-(2) N=8 n (%)	Dose Group-(3) N=7 n (%)	Placebo/ Secukinumab N=3 n (%)	Total N=39 n (%)
Patients with AE(s)	21 (100.0)	6 (75.0)	6 (85.7)	3 (100.0)	36 (92.3)
Infections and infestations	16 (76.2)	5 (62.5)	4 (57.1)	2 (66.7)	27 (69.2)
Musculoskeletal and connective tissue disorders	8 (38.1)	3 (37.5)	2 (28.6)	2 (66.7)	15 (38.5)
Gastrointestinal disorders	11 (52.4)	0	2 (28.6)	1 (33.3)	14 (35.9)
Nervous system disorders	5 (23.8)	0	3 (42.9)	1 (33.3)	9 (23.1)
Respiratory, thoracic and mediastinal disorders	5 (23.8)	3 (37.5)	1 (14.3)	0	9 (23.1)
Eye disorders	4 (19.0)	2 (25.0)	1 (14.3)	1 (33.3)	8 (20.5)
General disorders and administration site conditions	5 (23.8)	2 (25.0)	0	1 (33.3)	8 (20.5)
Injury, poisoning and procedural complications	3 (14.3)	3 (37.5)	1 (14.3)	1 (33.3)	8 (20.5)
Skin and subcutaneous tissue disorders	3 (14.3)	1 (12.5)	1 (14.3)	0	5 (12.8)
Cardiac disorders	1 (4.8)	2 (25.0)	1 (14.3)	0	4 (10.3)
Investigations	2 (9.5)	0	0	2 (66.7)	4 (10.3)
Psychiatric disorders	2 (9.5)	1 (12.5)	1 (14.3)		4 (10.3)
Vascular disorders	2 (9.5)	1 (12.5)		1 (33.3)	4 (10.3)
Renal and urinary disorders	1 (4.8)	0	1 (14.3)	1 (33.3)	3 (7.7)
Blood and lymphatic system disorders	2 (9.5)	0	0	0	2 (5.1)
Reproductive system and breast disorders	1 (4.8)	1 (12.5)	0	0	2 (5.1)
Ear and labyrinth disorders	0	1 (12.5)	0	0	1 (2.6)
Hepatobiliary disorders	1 (4.8)	0	0	0	1 (2.6)
Immune system disorders	1 (4.8)	0	0	0	1 (2.6)
Metabolism and nutrition disorders	1 (4.8)	0	0	0	1 (2.6)

Treatment received in core study: (1) secukinumab 2x10mg/kg, (2) secukinumab 2x1.0mg/kg, (3) secukinumab 2x0.1mg/kg

Arranged by frequency in the total column

Most Frequently Reported AEs Overall by Preferred Term n (%)

	Dose Group-(1) N=21 n (%)	Dose Group-(2) N=8 n (%)	Dose Group-(3) N=7 n (%)	Placebo/ Secukinumab N=3 n (%)	Total N=39
Patients with AE(s)	21 (100.0)	6 (75.0)	6 (85.7)	3 (100.0)	36 (92.3)
Nasopharyngitis	10 (47.6)	0	2 (28.6)	2 (66.7)	14 (35.9)
Fatigue	3 (14.3)	2 (25.0)		1 (33.3)	6 (15.4)
Oropharyngeal pain	3 (14.3)	2 (25.0)	1 (14.3)	0	6 (15.4)
Arthralgia	2 (9.5)	0	2 (28.6)	0	4 (10.3)

	Dose Group-(1) N=21 n (%)	Dose Group-(2) N=8 n (%)	Dose Group-(3) N=7 n (%)	Placebo/ Secukinumab N=3 n (%)	Total N=39
Diarrhoea	3 (14.3)	0		1 (33.3)	4 (10.3)
Headache	1 (4.8)	0	2 (28.6)	1 (33.3)	4 (10.3)
Influenza like illness	3 (14.3)	1 (12.5)	0		4 (10.3)
Iritis	2 (9.5)	1 (12.5)	0	1 (33.3)	4 (10.3)
Palpitations	1 (4.8)	2 (25.0)	1 (14.3)		4 (10.3)
Abdominal distension	2 (9.5)	0	1 (14.3)		3 (7.7)
Abdominal pain	3 (14.3)	0	0		3 (7.7)
Abdominal pain upper	2 (9.5)	0	0	1 (33.3)	3 (7.7)
Aphthous stomatitis	2 (9.5)	0	1 (14.3)		3 (7.7)
Back pain	2 (9.5)	0	0	1 (33.3)	3 (7.7)
Neck pain	1 (4.8)	1 (12.5)	0	1 (33.3)	3 (7.7)
Oedema peripheral	2 (9.5)	1 (12.5)	0	0	3 (7.7)
Sinusitis	2 (9.5)	0	1 (14.3)	0	3 (7.7)
Arthritis	1 (4.8)	1 (12.5)	0	0	2 (5.1)
Bronchitis	2 (9.5)	0	0	0	2 (5.1)
Bursitis	0	1 (12.5)	1 (14.3)	0	2 (5.1)
Contusion	1 (4.8)	0	0	1 (33.3)	2 (5.1)
Cough	1 (4.8)	1 (12.5)	0	0	2 (5.1)
Folliculitis	1 (4.8)	1 (12.5)	0	0	2 (5.1)
Gastroenteritis	2 (9.5)	0	0	0	2 (5.1)
Hypertension	1 (4.8)	0	0	1 (33.3)	2 (5.1)
Infected dermal cyst	0	1 (12.5)	1 (14.3)	0	2 (5.1)
Influenza	0	2 (25.0)	0	0	2 (5.1)
Iron deficiency anaemia	2 (9.5)	0	0	0	2 (5.1)
Joint injury	0	1 (12.5)	1 (14.3)	0	2 (5.1)
Nephrolithiasis	0	0	1 (14.3)	1 (33.3)	2 (5.1)
Paraesthesia	1 (4.8)	0	1 (14.3)	0	2 (5.1)
Pyrexia	1 (4.8)	1 (12.5)	0	0	2 (5.1)
Rash	2 (9.5)	0	0	0	2 (5.1)
Respiratory tract infection	1 (4.8)	0	0	1 (33.3)	2 (5.1)
Tendonitis	1 (4.8)	1 (12.5)	0	0	2 (5.1)
Toothache	1 (4.8)	0	1 (14.3)	0	2 (5.1)
Vomiting	2 (9.5)	0	0	0	2 (5.1)

Treatment received in core study: (1) secukinumab 2x10mg/kg, (2) secukinumab 2x1.0mg/kg, (3) secukinumab 2x0.1mg/kg

Arranged by frequency in the total column

Serious Adverse Events and Deaths

	Dose Group-(1) N=21 n (%)	Dose Group-(2) N=8 n (%)	Dose Group-(3) N=7 n (%)	Placebo/ Secukinumab N=3 n (%)	Total N=39 n (%)
Deaths	0	0	0	0	0

	Dose Group-(1) N=21 n (%)	Dose Group-(2) N=8 n (%)	Dose Group-(3) N=7 n (%)	Placebo/ Secukinumab N=3 n (%)	Total N=39 n (%)
Patients with SAE(s)	4 (19.0)	1 (12.5)	0	0	5 (12.8)
	0	0	0	0	0
Arthritis	1 (4.8)	0	0	0	1 (2.6)
Crohn's disease	1 (4.8)	0	0	0	1 (2.6)
Depression	1 (4.8)	0	0	0	1 (2.6)
Folliculitis	0	1 (12.5)	0	0	1 (2.6)
Sinusitis	1 (4.8)		0	0	1 (2.6)
Staphylococcal abscess	0	1 (12.5)	0	0	1 (2.6)

Treatment received in core study: (1) secukinumab 2x10mg/kg, (2) secukinumab 2x1.0mg/kg, (3) secukinumab 2x0.1mg/kg

Other Relevant Findings

None

Date of Clinical Trial Report

23 July 2013

Date Inclusion on Novartis Clinical Trial Results Database

25 Oct 2013

Date of Latest Update