Novartis Clinical Trials Results Database Template

Release date: 14 October 2011

Sponsor Novartis
Generic Drug Name AIN457
Therapeutic Area of Trial Moderate to severe chronic plaque-type psoriasis

Approved Indication

Investigational

Study Number

CAIN457A2211

Title

A randomized, double-blind, placebo controlled, multicenter regimen finding study of subcutaneously administered AIN457, assessing Psoriasis Area and Severity Index (PASI) response in patients with moderate to severe chronic plaque-type psoriasis

Phase of Development

Phase II

Study Start/End Dates

28-Jul-2009 to 16-Dec-2010

Study Design/Methodology

This multicenter study used a parallel-group, randomized, double-blind design. The study consisted of 4 periods: the screening period, the induction period, the maintenance period and the follow-up period. The screening period of 4 weeks was used to assess eligibility and to taper patients off disallowed medications. The purpose of the present study was to determine whether, in patients with moderate to severe plaque-type psoriasis, secukinumab (AIN457) administered subcutaneously reduced the severity of psoriasis symptoms (compared to placebo). Patients were exposed to different dose regimens during the trial, which consequently resulted in different serum exposure profiles for secukinumab (AIN457) over time for every dosing regimen.

Centres

A total of 60 centers: France (2 centers), Germany (13), Iceland (1), Israel (3), Japan (10), Norway (3) and United States (28).

Publication

None

Objectives

Primary objective

- To evaluate the efficacy of three induction regimens of secukinumab (AIN457) administered subcutaneously in patients with moderate to severe chronic plaque-type psoriasis with respect to PASI 75 achievement after 12 weeks of treatment, compared to placebo.

Key secondary objectives

- To compare the efficacy of two maintenance regimens of secukinumab (AIN457) with respect to PASI 75 achievement at least once from Week 21 to 29
- To evaluate the efficacy in three induction regimens of secukinumab (AIN457) administered subcutaneously as assessed by IGA (static IGA) after 12 weeks of treatment, compared to placebo.

Other secondary objectives

- To evaluate the efficacy of three induction regimens of secukinumab (AIN457) administered subcutaneously with respect to PASI 50 and PASI 90 achievement after 12 weeks of treatment, compared to placebo.
- To explore the effects of secukinumab (AIN457) treatment as assessed by IGA (static) over time during the trial up to 4 weeks after last study drug administration
- To evaluate the effects of treatment with secukinumab (AIN457) on PASI over time during the trial up to 4 weeks after last study drug administration
- To investigate the effects of treatment with secukinumab (AIN457) with respect to changes in DLQI over time during the trial up to 4 weeks after last study drug administration
- To investigate the effects of treatment with secukinumab (AIN457) with respect to DLQI 0 or 1 achievement over time during the trial up to 4 weeks after last study drug administration
- To investigate the clinical safety and tolerability of secukinumab (AIN457) as assessed by vitals signs, clinical laboratory variables, and adverse events monitoring.
- To investigate the time to start of relapse after the last dose of secukinumab (AIN457) administered in the induction period
- To investigate the proportion of non-responders who achieve a PASI 75 response after switching to the open label phase.
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Test Product (s), Dose(s), and Mode(s) of Administration

The dosage used was 150 mg of secukinumab (AIN457)/injection subcutaneously.

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

AIN457 Placebo to 150 mg Powder for Solution.

Criteria for Evaluation

Efficacy:

- Psoriasis Area and Severity Index (PASI)
- Investigator's Global Assessment (IGA) for overall psoriatic disease
- Investigator's Global Assessment (IGA) for involvement of hands and feet
- Dermatology Life Quality Index (DLQI)
- EQ-5D quality of life instrument
- Nail scoring
- Visual Analog Scales (VAS) for patient's assessment of pruritus and psoriatic arthritis
- Assessments for metabolic syndrome: weight, hip / waist circumference, blood pressure, fasting plasma glucose, lipids profile

Safety:

- AEs, SAEs, with their severity and relationship to study drug, and pregnancies
  - Clinical laboratory assessments (hematology, biochemistry)
  - Vital signs
  - Injection site as well as overall body examination
  - Recording of adverse events
  - Development of anti-AIN457-antibodies (immunogenicity)

Pharmacology

Not applicable

Other

- Pharmacokinetics and total IL-17 data
- Exploratory biomarker assessments
- Photographs of the overall body and target lesions at selected sites

Statistical Methods

All efficacy analyses were based on the full analysis set comprising all subjects who were randomized at Visit 2. The primary efficacy endpoint, achievement of PASI 75 at Week 13 (i.e. after 12 weeks of treatment), was analyzed by Dunnett's test procedure for proportions in a sequential manner to test the three null hypotheses, that the proportion of PASI 75 achievers in the active treatment arm was equal to the corresponding proportion in the placebo arm. Summary statistics were provided for PASI 75 response at Week 13. In additional sensitivity analysis PASI 75 at Week 13 was analyzed by means of the stratified Cochran-Mantel-Haenszel (CMH) test with region and body weight as strata for each pairwise comparison of treatment groups. In supplement, logistic regression model accounting for treatment group, region, body weight stratum and baseline PASI was applied. Odds ratios, 2-sided

95% confidence intervals and p-values for each pairwise treatment comparison were provided.

The two maintenance regimens Fixed Interval (FI) and Start of Relapse (SR) were compared by applying the stratified CMH test with region and body weight as stratum for PASI 75 achievement at least once from Week 21 to 29.

PASI 50, PASI 90, and IGA response were summarized with descriptive statistics over time for both the induction and maintenance periods. In addition, the same analyses as for the primary efficacy endpoint were carried out. Patient's assessment of psoriatic arthritis and pruritus, fingernail score and IGA of hands and feet were summarized descriptively for the induction and maintenance periods. Kaplan-Meier estimates of the probability of relapse were provided. Time to start of relapse was analyzed using a stratified log-rank test and a stratified Cox regression using body weight as stratum. The incidence of metabolic syndrome at baseline was cross-tabulated versus the incidence of metabolic syndrome at 4 weeks after last study drug administration. The number and percentage of patients experiencing rebound were presented by treatment group and visit.

The DLQI scores were summarized over time together with the percentage change from baseline by treatment group. Summary statistics were provided for the number of patients achieving DLQI 0 or 1. Treatment groups were compared by Fisher's exact test. The absolute value and the percentage change from baseline of DLQI total score were analyzed with the Van-Elteren test for all pairwise comparisons between treatment groups at each visit. Stratified Hodges-Lehmann estimates for the median and 95% confidence intervals were derived.

The number and percentage of patients in each of the EQ-5D categories were summarized by visit and treatment group. The health state assessment was summarized with summary statistics.

All safety analyses were done on the safety set and comprised descriptive summaries of adverse events, vital signs, and clinical laboratory values. All summaries were provided by treatment group separately for the induction and maintenance periods. Criteria for potential clinically notable laboratory values and vital signs were applied and summarized. Potential risks (infections, malignancies, hypersensitivity, lack of efficacy, antibody development, risk during pregnancy) were defined based on adverse events and summarized. Relative risks were calculated with 95% confidence intervals for each potential risk and each of the active treatment groups with placebo as reference. Time to first infection was analyzed using stratified log-rank tests stratified by body weight stratum.

Summary statistics were provided for anti-AIN 457 antibodies as well as for the assessment immunogenicity (yes /no) by treatment group and visit.

Study Population: Inclusion/Exclusion Criteria and Demographics

It was aimed to randomize a total of 396 patients in around 85 centers worldwide. Approximately 566 patients were expected to be screened to provide the number of randomized patients. A total 404 patients were randomized and treated during this period, of whom 380 (94.1%) completed this period.

Patients eligible for inclusion in this study had to fulfill all of the following criteria:

- Men or women at least 18 years of age at time of consent.
- Chronic plaque-type psoriasis diagnosed for at least 6 months at time of randomization

At randomization, moderate to severe psoriasis as defined by:

- PASI score of 12 or greater and,
- IGA score of 3 or greater and,
- Body Surface Area (BSA) affected by plaque-type psoriasis of 10% or greater
- At screening and randomization, chronic plaque-type psoriasis considered inadequately controlled by:
- topical treatment

In addition, patients may have failed to respond to:

- phototherapy and/or
- previous systemic therapy
- Male patients had to consent to practice reliable contraception during the study and for 16 weeks after the last dose of study drug administration.
- Patient had to be able to understand and communicate with the investigator and comply with the requirements of the study and give a written, signed and dated informed consent before any study related activity was performed.

Key exclusion criteria were: Patients with any other forms of psoriasis other than chronic plaque-type (e.g., pustular, erythrodermic and guttate psoriasis, drug-induced psoriasis), ongoing use of prohibited psoriasis and other treatments (e.g., topical or systemic corticosteroids, UV therapy), known immunosuppression (e.g., AIDS), history or evidence of active tuberculosis (unless sufficient treatment was initiated according to local regulations), active systemic infections (other than common cold; e.g., hepatitis), malignancy of any organ system within the past 5 years, congestive heart failure (NYHA functional classification ≥ III), severe hypersensitivity to any human or humanized biological agents, live vaccination within prior 6 weeks, pregnant or nursing (lactating) women or women of child-bearing potential using a highly effective method of birth control (reliable contraception was to be maintained for male and females patients throughout the study).

Number of Subjects

Patient disposition in induction period (Randomized set)

	Single N=66 n (%)	Monthly N=138 n (%)	Early N=133 n (%)	Placebo N=67 n (%)	Total N=404 n (%)
Patients					
Randomized	66 (100.0)	138 (100.0)	133 (100.0)	67 (100.0)	404 (100.0)
Randomized and treated	66 (100.0)	138 (100.0)	133 (100.0)	67 (100.0)	404 (100.0)
Completed induction period	61 (92.4)	134 (97.1)	127 (95.5)	58 (86.6)	380 (94.1)
Discontinued induction period	5 (7.6)	4 (2.9)	6 (4.5)	9 (13.4)	24 (5.9)
Primary reason for premature discontinuation					
Unsatisfactory therapeutic effect	2 (3.0)	1 (0.7)	0 (0.0)	5 (7.5)	8 (2.0)
Patient withdrew consent	1 (1.5)	2 (1.4)	2 (1.5)	2 (3.0)	7 (1.7)
Adverse Event(s)	1 (1.5)	0 (0.0)	3 (2.3)	2 (3.0)	6 (1.5)
Administrative problems	1 (1.5)	1 (0.7)	1 (0.8)	0 (0.0)	3 (0.7)

Patients with an assessment of PASI score on Visit 7 (Week 13) are defined as completers of induction period.

Patient disposition in maintenance period (Randomized set)

	Fixed interval N=65 n (%)	Start of relapse N=67 n (%)	Open label N=247 n (%)	Total N=379 n (%)
Patients				
Randomized	65 (100.0)	67 (100.0)	247 (100.0)	379 (100.0)
Randomized and treated	65 (100.0)	67 (100.0)	247 (100.0)	379 (100.0)
Completed	56 (86.2)	61 (91.0)	204 (82.6)	321 (84.7)
Discontinued maintenance period	9 (13.8)	6 (9.0)	43 (17.4)	58 (15.3)
Primary reason for premature discontinuation				
Patient withdrew consent	6 (9.2)	2 (3.0)	13 (5.3)	21 (5.5)
Unsatisfactory therapeutic effect	0 (0.0)	0 (0.0)	13 (5.3)	13 (3.4)
Lost to follow-up	2 (3.1)	2 (3.0)	7 (2.8)	11 (2.9)
Adverse Event(s)	0 (0.0)	2 (3.0)	8 (3.2)	10 (2.6)
Administrative problems	1 (1.5)	0 (0.0)	1 (0.4)	2 (0.5)
Protocol deviation	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.3)

1 patient discontinued right after induction period

Demographic and Background Characteristics

Demographics and baseline characteristics, by induction treatment (Randomized set)

		Single N=66	Monthly N=138	Early N=133	Placebo N=67	Total N=404
Age (years)	n	66	138	133	67	404
	Mean	42.7	44.2	44.5	44.2	44.1
	SD	11.32	12.96	12.45	12.59	12.44
	Median	43.0	43.0	45.0	45.0	44.0
	Min - Max	21 - 69	18 - 73	20 - 77	18 - 74	18 - 77
Age group - n (%)	18-44 years	36 (54.5)	73 (52.9)	65 (48.9)	33 (49.3)	207 (51.2)
	45-64 years	27 (40.9)	58 (42.0)	62 (46.6)	30 (44.8)	177 (43.8)
	65-74 years	3 (4.5)	7 (5.1)	4 (3.0)	4 (6.0)	18 (4.5)
	≥ 75 ye rs	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	2 (0.5)
Sex - n (%)	Male	53 (80.3)	104 (75.4)	105 (78.9)	44 (65.7)	306 (75.7)
	Female	13 (19.7)	34 (24.6)	28 (21.1)	23 (34.3)	98 (24.3)
Race - n (%)	Caucasian	59 (89.4)	120 (87.0)	118 (88.7)	56 (83.6)	353 (87.4)
	Black	0 (0.0)	1 (0.7)	0 (0.0)	1 (1.5)	2 (0.5)
	Asian	7 (10.6)	17 (12.3)	14 (10.5)	8 (11.9)	46 (11.4)
	Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	1 (0.2)
	Other	0 (0.0)	0 (0.0)	1 (0.8)	1 (1.5)	2 (0.5)
Body weight - n (%)	< 90 kg	32 (48.5)	68 (49.3)	70 (52.6)	34 (50.7)	204 (50.5)
	≥ 90 kg	34 (51.5)	70 (50.7)	63 (47.4)	33 (49.3)	200 (49.5)
BMI (kg/m^2)	n	66	138	133	67	404
	Mea	30.5	30.9	29.4	31.9	30.5
	SD	7.31	6.90	6.71	9.51	7.42
	Median	28.4	29.6	28.6	29.6	29.0
	Min - Max	17.1 - 51.7	18.9 - 53.0	16. - 52.6	16.7 - 59.1	16.6 - 59.1
Time since first diagnosis of psoriasis (years)	n	66	138	133	67	404
	Mean	17.5	16.9	17.4	15.4	16.9
	SD	10.05	11.47	11.82	10.70	11.23
	Median	16.9	14.5	16.3	14.3	15.4
	Min - Max	0.8 - 41.1	0.7 - 49.5	0.7 - 50.5	0.7 - 37.3	0.7 - 50.5
Psoriatic arthritis present - n (%)	No	51 (77.3)	93 (67.4)	94 (70.7)	55 (82.1)	293 (72.5)
	Yes	15 (22.7)	45 (32.6)	39 (29.3)	12 (17.9)	111 (27.5)

PASI score	n	66	138	133	67	404
	Mean	19.9	20.8	19.9	20.5	20.3
	SD	6.73	8.08	7.81	9.31	7.99
	Median	18.3	18.0	17.7	17.6	17.8
	Min - Max	12.1 - 41.9	11.4 - 52.3	8.2 - 47.3	12.0 - 56.5	8.2 - 56.5
IGA for overall psoriatic disease - n (%)	Clear	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Almost clear	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Mild disease	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Moderate disease	28 (42.4)	64 (46.4)	65 (48.9)	26 (38.8)	183 (45.3)
	Severe disease	35 (53.0)	62 (44.9)	62 (46.6)	34 (50.7)	193 (47.8)
	Very severe disease	3 (4.5)	12 (8.7)	6 (4.5)	7 (10.4)	28 (6.9)

BMI = Body mass index (= weight [kg] / height [m]^2), IGA = Investigator's Global Assessment

Primary Objective Result(s)

PASI 75 response (%) at Week 13: treatment comparison vs. placebo (Full analysis set, LOCF)

Comparison	LS Mean (%)	SE	Adjusted p-value
Single vs. placebo	9.09	7.485	0.225
Monthly vs. placebo	40.51	6.435	<.001
Early vs. placebo	53.03	6.483	<.001

LS Mean = least squares mean (of difference in proportions), SE= standard error of the mean

Number (%) of patients achieving PASI 50, PASI 75, PASI 90, by visit and induction treatment (Full analysis set, LOCF)

Visit	Criterion	Single N=66 n (%)	Monthly N=138 n (%)	Early N=133 n (%)	Placebo N=67 n (%)	Total N=404 n (%)
Week 13	n evaluable	66	138	132	66	402
	PASI 50	18 (27.3)	83 (60.1)	101 (76.5)	7 (10.6)	209 (52.0)
	PASI 75	7 (10.6)	58 (42.0)	72 (54.5)	1 (1.5)	138 (34.3)
	PASI 90	2 (3.0)	24 (17.4)	42 (31.8)	1 (1.5)	69 (17.2)

Secondary Objective Result(s)

PASI 75 achievement at least once from Week 21 to Week 29 (Full analysis set, LOCF)

Comparison	p-value (CMH test)
Fixed interval vs. Start of relapse	0.020

Visit	Criterion	Fixed interval N=65 n (%)	Start of relapse N=67 n (%)	Open label N=247 n (%)
At any time from Week 21 to Week 29	n evaluable	65	67	247
	PASI 50	64 (98.5)	60 (89.6)	200 (81.0)
	PASI 75	55 (84.6)	45 (67.2)	114 (46.2)
	PASI 90	38 (58.5)	14 (20.9)	53 (21.5)

Investigator's Global Assessment (IGA), by visit and induction treatment (Full analysis set, LOCF)

Visit	Statistic	Single N=66	Monthly N=138	Early N=133	Placebo N=67	Total N=404
Week 13	n evaluable	66	137	132	66	401
	Response, n (%)	3 (4.5)	31 (22.6)	49 (37.1)	1 (1.5)	84 (20.9)
	Odds ratio vs. plac.	3.08	21.20	43.31		
	95% CI of odds ratio	(0.31, 30.91)	(2.78, 161.52)	(5.72, 328.25)		
	p-value vs. placebo	0.338	0.003	<.001		

Response was defined as an IGA score of 0 (clear) or 1 (almost clear) and improvement of at least 2 points on the IGA scale compared to baseline.
Odds ratios and their confidence intervals and p-values are based on a logistic regression model:
IGA response = treatment group + region + body weight stratum + baseline IGA.
An odds ratio > 1 favors the treatment group in the numerator of the ratio (i.e., the active dose).

Safety Results

Adverse Events by System Organ Class

Adverse events overall and by primary system organ class, by and during induction treatment- n (%) of patients (Safety set)

	Single N=66 n (%)	Monthly N=138 n (%)	Early N=133 n (%)	Placebo N=67 n (%)	Total N=404 n (%)
Patients with any AE(s)	41 (62.1)	91 (65.9)	89 (66.9)	47 (70.1)	268 (66.3)
Primary SOC					
Infections and infestations	14 (21.2)	56 (40.6)	45 (33.8)	26 (38.8)	141 (34.9)
Skin and subcutaneous tissue disorders	14 (21.2)	15 (10.9)	13 (9.8)	11 (16.4)	53 (13.1)
Gastrointestinal disorders	6 (9.1)	14 (10.1)	16 (12.0)	7 (10.4)	43 (10.6)
Nervous system disorders	7 (10.6)	10 (7.2)	13 (9.8)	6 (9.0)	36 (8.9)
Musculoskeletal and connective tissue disorders	6 (9.1)	16 (11.6)	6 (4.5)	5 (7.5)	33 (8.2)
General disorders and administration site conditions	6 (9.1)	10 (7.2)	12 (9.0)	4 (6.0)	32 (7.9)
Respiratory, thoracic and mediastinal disorders	4 (6.1)	6 (4.3)	10 (7.5)	6 (9.0)	26 (6.4)
Injury, poisoning and procedural complications	5 (7.6)	6 (4.3)	12 (9.0)	2 (3.0)	25 (6.2)
Investigations	2 (3.0)	6 (4.3)	6 (4.5)	4 (6.0)	18 (4.5)
Vascular disorders	3 (4.5)	3 (2.2)	4 (3.0)	2 (3.0)	12 (3.0)
Eye disorders	1 (1.5)	4 (2.9)	3 (2.3)	2 (3.0)	10 (2.5)
Metabolism and nutrition disorders	2 (3.0)	4 (2.9)	2 (1.5)	1 (1.5)	9 (2.2)
Psychiatric disorders	0 (0.0)	2 (1.4)	2 (1.5)	4 (6.0)	8 (2.0)
Ear and labyrinth disorders	0 (0.0)	4 (2.9)	1 (0.8)	2 (3.0)	7 (1.7)
Reproductive system and breast disorders	1 (1.5)	1 (0.7)	1 (0.8)	2 (3.0)	5 (1.2)
Cardiac disorders	1 (1.5)	0 (0.0)	3 (2.3)	0 (0.0)	4 (1.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (3.0)	2 (1.4)	0 (0.0)	0 (0.0)	4 (1.0)
Renal and urinary disorders	0 (0.0)	1 (0.7)	2 (1.5)	0 (0.0)	3 (0.7)
Hepatobiliary disorders	0 (0.0)	1 (0.7)	0 (0.0)	1 (1.5)	2 (0.5)
Blood and lymphatic system disorders	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.2)
Immune system disorders	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.2)

Primary SOCs are sorted in the descending frequency for the total column.

Adverse events overall and by primary system organ class, by and during maintenance treatment - n (%) of patients (Safety set)

	Fixed interval N=65 n (%)	Start of relapse N=67 n (%)	Open label N=247 n (%)	Total N=379 n (%)
Patients with any AE(s)	43 (66.2)	43 (64.2)	167 (67.6)	253 (66.8)
Primary SOC				
Infections and infestations	19 (29.2)	15 (22.4)	87 (35.2)	121 (31.9)
Skin and subcutaneous tissue disorders	7 (10.8)	10 (14.9)	35 (14.2)	52 (13.7)
Musculoskeletal and connective tissue disorders	13 (20.0)	9 (13.4)	26 (10.5)	48 (12.7)
Gastrointestinal disorders	8 (12.3)	6 (9.0)	30 (12.1)	44 (11.6)
Nervous system disorders	6 (9.2)	4 (6.0)	23 (9.3)	33 (8.7)
Respiratory, thoracic and mediastinal disorders	6 (9.2)	4 (6.0)	22 (8.9)	32 (8.4)
General disorders and administration site conditions	8 (12.3)	3 (4.5)	18 (7.3)	29 (7.7)
Injury, poisoning and procedural complications	7 (10.8)	5 (7.5)	17 (6.9)	29 (7.7)
Investigations	4 (6.2)	2 (3.0)	17 (6.9)	23 (6.1)
Vascular disorders	4 (6.2)	5 (7.5)	5 (2.0)	14 (3.7)
Metabolism and nutrition disorders	1 (1.5)	2 (3.0)	9 (3.6)	12 (3.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	3 (4.6)	1 (1.5)	8 (3.2)	12 (3.2)
Psychiatric disorders	0 (0.0)	2 (3.0)	8 (3.2)	10 (2.6)
Eye disorders	3 (4.6)	1 (1.5)	5 (2.0)	9 (2.4)
Renal and urinary disorders	0 (0.0)	1 (1.5)	6 (2.4)	7 (1.8)
Blood and lymphatic system disorders	1 (1.5)	1 (1.5)	3 (1.2)	5 (1.3)
Cardiac disorders	0 (0.0)	0 (0.0)	5 (2.0)	5 (1.3)
Ear and labyrinth disorders	1 (1.5)	0 (0.0)	4 (1.6)	5 (1.3)
Hepatobiliary disorders	1 (1.5)	0 (0.0)	4 (1.6)	5 (1.3)
Immune system disorders	0 (0.0)	1 (1.5)	4 (1.6)	5 (1.3)
Reproductive system and breast disorders	0 (0.0)	1 (1.5)	4 (1.6)	5 (1.3)
Congenital, familial and genetic disorders	1 (1.5)	0 (0.0)	0 (0.0)	1 (0.3)
Endocrine disorders	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.3)

Primary SOCs are sorted in the descending frequency for the total column.

Most Frequently Reported AEs Overall by Preferred Term by induction treatment n (%) of patients (Safety set), 10 highest total frequencies

Patients with any AE(s)	41 (62.1)	91 (65.9)	89 (66.9)	47 (70.1)	268 (66.3)
Preferred term					
Nasopharyngitis	8 (12.1)	31 (22.5)	30 (22.6)	12 (17.9)	81 (20.0)
Headache	6 (9.1)	8 (5.8)	11 (8.3)	3 (4.5)	28 (6.9)
Psoriasis*	6 (9.1)	8 (5.8)	4 (3.0)	7 (10.4)	25 (6.2)
Upper respiratory tract infection	3 (4.5)	6 (4.3)	2 (1.5)	6 (9.0)	17 (4.2)
Cough	1 (1.5)	2 (1.4)	4 (3.0)	4 (6.0)	11 (2.7)
Arthralgia	2 (3.0)	8 (5.8)	0 (0.0)	0 (0.0)	10 (2.5)

Vomiting	3 (4.5)	3 (2.2)	3 (2.3)	1 (1.5)	10 (2.5)
Toothache	0 (0.0)	2 (1.4)	5 (3.8)	2 (3.0)	9 (2.2)
Pruritus generalized	1 (1.5)	4 (2.9)	1 (0.8)	2 (3.0)	8 (2.0)
Hypertension	3 (4.5)	1 (0.7)	2 (1.5)	1 (1.5)	7 (1.7)
Oropharyngeal pain	2 (3.0)	2 (1.4)	2 (1.5)	1 (1.5)	7 (1.7)
Pruritus	2 (3.0)	3 (2.2)	1 (0.8)	1 (1.5)	7 (1.7)

* The protocol suggested that psoriasis being the studied indication was not to be reported as an AE by the investigators.
Preferred terms are sorted in descending order of frequency in the total treatment group.

Most Frequently Reported AEs Overall by Preferred Term by maintenance treatment n (%) of patients (Safety set), 10 highest total frequencies

	Fixed interval N=65 n (%)	Start of relapse N=67 n (%)	Open label N=247 n (%)	Total N=379 n (%)
Patients with any AE(s)	43 (66.2)	43 (64.2)	167 (67.6)	253 (66.8)
Preferred term				
Nasopharyngitis	6 (9.2)	5 (7.5)	35 (14.2)	46 (12.1)
Psoriasis	4 (6.2)	6 (9.0)	17 (6.9)	27 (7.1)
Upper respiratory tract infection	2 (3.1)	0 (0.0)	17 (6.9)	19 (5.0)
Headache	3 (4.6)	1 (1.5)	13 (5.3)	17 (4.5)
Back pain	4 (6.2)	3 (4.5)	9 (3.6)	16 (4.2)
Hypertension	2 (3.1)	5 (7.5)	5 (2.0)	12 (3.2)
Arthralgia	1 (1.5)	1 (1.5)	9 (3.6)	11 (2.9)
Fatigue	3 (4.6)	2 (3.0)	4 (1.6)	9 (2.4)
Pyrexia	1 (1.5)	2 (3.0)	6 (2.4)	9 (2.4)
Cough	0 (0.0)	0 (0.0)	8 (3.2)	8 (2.1)
Oropharyngeal pain	2 (3.1)	1 (1.5)	5 (2.0)	8 (2.1)

Preferred terms are sorted in descending order of frequency in the total treatment group.

Serious Adverse Events and Deaths

Deaths, other serious adverse events and adverse events leading to permanent discontinuation of study drug, by induction treatment - n (%) of patients (Safety set)

	Single N=66 n (%)	Monthly N=138 n (%)	Early N=133 n (%)	Placebo N=67 n (%)	Total N=404 n (%)
Patients with any AE(s)	41 (62.1)	91 (65.9)	89 (66.9)	47 (70.1)	268 (66.3)
SAEs or AE discontinuations					
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
SAE(s)	3 (4.5)	3 (2.2)	6 (4.5)	1 (1.5)	13 (3.2)
Discontinued due to AE(s)	1 (1.5)	0 (0.0)	3 (2.3)	1 (1.5)	5 (1.2)

Deaths, other serious adverse events and adverse events leading to permanent discontinuation of study drug, by maintenance treatment - n (%) of patients (Safety set)

	Fixed interval N=65 n (%)	Start of relapse N=67 n (%)	Open label N=247 n (%)	Total N=379 n (%)
Patients with any AE(s)	43 (66.2)	43 (64.2)	167 (67.6)	253 (66.8)
SAEs or AE discontinuations				
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
SAE(s)	4 (6.2)	2 (3.0)	12 (4.9)	18 (4.7)
Discontinued due to AE(s)	0 (0.0)	2 (3.0)	8 (3.2)	10 (2.6)

Follow-Up period

The overall number of SAEs during Follow-Up period was 7 in 6 out of 127 patients. There were 4 malignancies reported (Monthly/Open Label group: Lung neoplasm malignant, Malignant melanoma in situ; Placebo/Open Label group: Bladder cancer (reported already for maintenance); Placebo: Breast cancer). For one patient having received the Placebo during induction and entered Open Label group in the maintenance there were an SAE of Ventricular fibrillation (Cardiac disorders) and an SAE of Septic shock (Infections and infestations) reported. For one patient having received the Monthly induction treatment and entered Open Label group in the maintenance there was an SAE of Psoriasis (Skin and subcutaneous tissue disorders).

Other Relevant Findings

NA

Date of Clinical Trial Report

TBD

Date Inclusion on Novartis Clinical Trial Results Database

14 December 2011

Date of Latest Update

14 December 2011