Sponsor

Novartis

Generic Drug Name

Secukinumab

Therapeutic Area of Trial

Uveitis

Approved Indication

Investigational

Study Number

CAIN457C2302 (core study) and CAIN457C2302E1 (extension study)

Title

A 28-week multicenter, randomized, double-masked, placebo controlled, dose-ranging phase III study to assess AIN457 versus placebo in inducing and maintaining uveitis suppression in adults with active, non-infectious, intermediate, posterior or panuveitis requiring immunosuppression including a 34-week extension (INSURE Study)

Phase of Development

Phase III

Study Start/End Dates

Study initiation date: First patient first visit for Study CAIN457C2302 was 13-Apr-2010. For Study CAIN457C2302E1, patients were enrolled only for the completion of the Visit 30/safety follow up. 19-Dec-2010 was the date that first patient reached Visit 30. No doses were administered in Study CAIN457C2302E1.

Early termination date: Study CAIN457C2302: 7-Oct-2010. Not applicable for Study CAIN457C2302E1

Study completion date: 27-Oct-2010 [last patient last visit (Visit 17/Early Discontinuation)]

10-Feb-2011 [last patient last visit (Visit 30)]

Study Design/Methodology

Study CAIN457C2302 was a 28-week multicenter, randomized, double-masked, placebo-controlled, dose-ranging study evaluating 3 doses of AIN457 (300 mg s.c. at baseline, Week 1 and Week 2, then every 2 weeks, 300 mg s.c. at baseline and Week 2, then every 4 weeks, and 150 mg s.c. at baseline and Week 2, then every 4 weeks) versus placebo (s.c at baseline, Week 1 and Week 2, then every 2 weeks) in inducing and maintaining uveitis

suppression in adults with active, non-infectious, intermediate, posterior or panuveitis requiring immunosuppression.

Study CAIN457C2302E1 was a 34-week extension study, which was intended to provide patients who completed the 28-week core study an opportunity to receive an additional 22 weeks of continuous study treatment. Because the study was prematurely terminated, patients were enrolled only for the completion of the Visit 30/safety follow up. No doses were administered in Study CAIN457C2302E1.

Centres

20 centers in 9 countries: Japan (8), US (3), Canada (2), Israel (2); Hungary, Singapore, France, Germany and Switzerland each had one center

Publication

None

Objectives

Primary objective(s)

The primary objective of Study CAIN4572302 was to evaluate the efficacy of three dose regimens of subcutaneous AIN457 compared to placebo when administered as an adjunctive therapy to standard-of-care immunosuppressive medications for inducing quiescence and maintaining quiescence during the withdrawal of concomitant immunosuppressive therapy in adults with active, non-infectious, intermediate uveitis, posterior uveitis or panuveitis.

The primary objective of Study CAIN4572302E1 was to evaluate the efficacy of continuous treatment with subcutaneous AIN457 compared to placebo for maintaining quiescence of intraocular inflammation and the prevention of active intermediate, posterior or panuveitis recurrences in adults with non-infectious, uveitis affecting the posterior segment.

Secondary objective(s)

The key secondary objective of Study CAIN4572302 was to determine if treatment with subcutaneous AIN457 can reduce or eliminate the need for standard of care immunosuppressive medications.

The key secondary objective of Study CAIN4572302E1 was to determine if continuous treatment with subcutaneous AIN457 can reduce/eliminate the need for concomitant standard-of-care immunosuppressive medications in patients requiring systemic immunosuppression to control their ocular inflammatory disease.

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

- AIN457 300 mg subcutaneously at baseline, Week 1 and Week 2, then every 2 weeks.
- AIN457 300 mg subcutaneously at baseline and Week 2, then every 4 weeks.
- AIN457 150 mg subcutaneously at baseline and Week 2, then every 4 weeks.

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

- Placebo administered subcutaneously to match the dosage regimen of AIN457.

Criteria for Evaluation

Primary variable

The original primary efficacy variable was the mean change in vitreous haze score in the study eye from baseline to 28 weeks or at time of rescue, if earlier. This criterion was modified at the time of analysis plan finalization to the mean change in vitreous haze score in the study eye from baseline to end of study. The revision of the analysis timepoint from 28 weeks to end of study also applied to the secondary efficacy variables (shown below), as applicable.

Secondary variables

Secondary efficacy variables were as follows:

- Time to response
- Mean change from baseline to end of study in:

  -vitreous haze in the fellow eye

  -immunosuppressive medication score

  -best corrected visual acuity (study eye & fellow eye)

  -anterior chamber cell grade (study eye & fellow eye)

  -foveal thickness as measured by optical coherence tomography (study eye & fellow eye)
- Proportion of patients with ≥ 15 Early Treatment Diabetic Retinopathy Study (ETDRS) letter gains or loss of visual acuity at end of study
- Immunosuppressive medications except topical (any site) before start of study drug
- Immunosuppressive medications except topical (any site) after start of study drug
- Topical immunosuppressive medications before start of study drug
- Topical immunosuppressive medications after start of study drug
- Visual Function Questionnaire (VFQ-25)

Safety and tolerability

Treatment-emergent adverse events (AEs), serious adverse events (SAEs), pregnancies, hematology, clinical chemistry, urine, vital signs, physical condition, height, and body weight, health-related quality of life assessments, immunogenicity.

Statistical Methods

The results of Study CAIN457C2303 (conducted in non-infectious uveitis patients with Behçet's disease) did not meet the primary endpoint. Due to the efficacy results observed in Study CAIN457C2303, the Sponsor prematurely terminated all enrollment in Study CAIN457C2302 and the subsequent 34-week Extension Study CAIN457C2302E1 (Study C2302E1) (Note: the study was not terminated for any safety reasons). No treatment was given for the extension; only the Visit 30 safety follow-up information was collected for patients as part of the extension.

As a result of early study termination, study CAIN457C2302 enrolled only 31 patients, and a substantial number of analyses initially planned in the protocol (particularly inferential analyses) were not performed or modified.

Data analysis comprised the analysis of data collected within the combined core (CAIN457C2302) and the extension study (CAIN457C2302E1). From the extension study only data of a safety follow up visit was collected and available for the analysis.

For all patients, only one eye was considered the study eye. For eye specific efficacy and safety parameters, the data of the study and the fellow eye were summarized.

Data were summarized with respect to demographic characteristics, efficacy outcomes, adverse events, and other safety data.

Descriptive statistics (n, mean, standard deviation, median, quartiles (optionally), minimum and maximum values for continuous variables, and frequencies and percentages for categorical variables) were provided where applicable by eye (study and fellow).

Where appropriate, the 2-sided 95%-confidence intervals were presented.

For statistical purposes, baseline was defined as the last available non-missing value collected just prior to the start of treatment including unscheduled visits and the screening visit.

Study Population: Inclusion/Exclusion Criteria and Demographics

Inclusion criteria:

- Male and female patients =18 years of age
- Active, non-infectious, intermediate uveitis, posterior uveitis or panuveitis requiring systemic immunosuppressive therapy

Exclusion criteria:

- Patients who received or required prednisone (or equivalent) =1.5 mg/kg/day for the treatment of their active uveitis
- Primary diagnosis of Behçet's disease, anterior uveitis, or any intermediate uveitis, posterior uveitis or panuveitis in which the manifestation(s) of the active intraocular inflammatory disease may spontaneously resolve or that was not characterized by the presence of either anterior chamber cells or vitritis (vitreous cell and haze) such as the white dot retino-choroidopathies (e.g. punctuate inner choroidopathy (PIC), acute zonal occult outer retinopathy (AZOOR).

Number of Subjects

Patient disposition (Randomized set)

Disposition/ Reason for discontinuation	AIN457 300 mg q 2 weeks N=8 n (%)	AIN457 300 mg q 4 weeks N=10 n (%)	AIN457 150 mg q 4 weeks N=8 n (%)	Placebo q 2 weeks N=5 n (%)
Continuing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Completed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Discontinued	8 (100.0)	10 (100.0)	8 (100.0)	5 (100.0)
Main cause of discontinuation				
Administrative problems	8 (100.0)	10 (100.0)	7 (87.5)	5 (100.0)
Adverse event(s)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abnormal laboratory value(s)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abnormal test procedure result	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Condition no long required study drug	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Subject withdrew consent	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)
Lost to follow-up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Protocol deviation	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

q = every. Percentages are calculated using the Randomized set as the denominator

Demographic and Background Characteristics

Demographics and background characteristics (Randomized set)

Characteristics		AIN457 300 mg q 2 weeks N=8 n (%)	AIN457 300 mg q 4 weeks N=10 n (%)	AIN457 150 mg q 4 weeks N=8 n (%)	Placebo q 2 weeks N=5 n (%)	Total N=31 n (%)
Age (years)	n	8	10	8	5	31
	Mean (SD)	47.5 (21.13)	46.9 (12.80)	44.6 (15.99)	50.6 (12.99)	47.1 (15.47)
	Median	49.5	48.5	40.5	52.0	49.0
	Range	19-80	25-67	21-72	30-66	19-80
Age group	55 < years	4 (50.0)	7 (70.0)	6 (75.0)	4 (80.0)	21 (67.7)
n (%)	55 - <65 years	3 (37.5)	2 (20.0)	1 (12.5)	0 (0.0)	6 (19.4)
	65 - <75 years	0 (0.0)	1 (10.0)	1 (12.5)	1 (20.0)	3 (9.7)
	= 7 years	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.2)
Gender	Male	4 (50.0)	4 (40.0)	6 (75.0)	2 (40.0)	16 (51.6)
n (%)	Female	4 (50.0)	6 (60.0)	2 (25.0)	3 (60.0)	15 (48.4)
Predom nant race	Caucasian	2 (25.0)	7 (70.0)	3 (37.5)	3 (60.0)	15 (48.4)
n (%	Black	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.2)
	Asian	5 (62.5)	3 (30.0)	4 (50.0)	2 (40.0)	14 (45.2)
	Other	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.2)
Ethnicity	Chinese	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.2)
n (%)	Japanese	4 (50.0)	3 (30.0)	4 (50.0)	2 (40.0)	13 (41.9)
	Mixed ethnicity	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.2)
	Other	3 (37.5)	7 (70.0)	3 (37.5)	3 (60.0)	16 (51.6)
Weight (kg)	n	8	10	8	5	31
	Mean (SD)	71.74 (21.64)	81.36 (24.56)	69.93 (18.55)	67.50 (20.03)	73.69 (21.33)
	Median	70.10	82.25	64.00	59.10	72.00
	Range	46.9-112.0	43.3-126.0	53.2-110.0	48.3-100.0	43.3-126.0

Percentages are based on the total number of patients in the Randomized set.

Ocular characteristics of the study eye at baseline (Randomized set)

Characteristics	AIN457 300mg q 2 weeks N=8	AIN457 300mg q 4 weeks N=10	AIN457 150mg q 4 weeks N=8	Placebo q 2 weeks N=5	Total N=31
Study eye selection - n (%)					
Left eye	4 (50.0)	8 (80.0)	2 (25.0)	5 (100.0)	19 (61.3)
Right eye	4 (50.0)	2 (20.0)	6 (75.0)	0 (0.0)	12 (38.7)
Type of uveitis - n (%)					
Intermediate uveitis	2 (25.0)	3 (30.0)	2 (25.0)	3 (60.0)	10 (32.3)
Posterior uveitis	2 (25.0)	1 (10.0)	1 (12.5)	0 (0.0)	4 (12.9)
Panuveitis	4 (50.0)	6 (60.0)	5 (62.5)	2 (40.0)	17 (54.8)
Anterior uveitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Visual acuity (letters)					
n	8	10	8	5	31
Mean (SD)	66.4 (15.91)	66.2 (9.86)	63.0 (16.73)	68.6 (7.06)	65.8 (12.80)
Median	68.5	66.5	64.5	70.0	69.0
Range	35 - 85	48 - 81	41 - 85	59 - 76	35 - 85
Vitreous haze score - n (%)					
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Trace (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (20.0)	1 (3.2)
1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2	7 (87.5)	7 (70.0)	8 (100.0)	3 (60.0)	25 (80.6)
3	1 (12.5)	3 (30.0)	0 (0.0)	1 (20.0)	5 (16.1)
4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anterior chamber cell - n (%)					
0	3 (37.5)	3 (30.0)	4 (50.0)	1 (20.0)	11 (35.5)
Trace (0.5)	3 (37.5)	4 (40.0)	0 (0.0)	1 (20.0)	8 (25.8)
1+	1 (12.5)	2 (20.0)	2 (25.0)	1 (20.0)	6 (19.4)
2+	1 (12.5)	1 (10.0)	2 (25.0)	0 (0.0)	4 (12.9)
3+	0 (0.0)	0 (0.0)	0 (0.0)	2 (40.0)	2 (6.5)
4+	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Central retinal thickness (um)					
n	8	10	8	5	31
Mean (SD)	313.9 (151.71)	304.4 (173.32)	419.9 (208.02)	334.0 (139.17)	341.4 (171.38)
Median	268.0	258.5	410.5	275.0	275.0
Range	171 - 665	155 - 782	175 - 795	246 - 581	155 - 795
Intraocular pressure (mmHg)					
n	8	10	8	5	31
Mean (SD)	16.0 (4.28)	11.9 (3.07)	14.8 (4.06)	14.4 (1.95)	14.1 (3.76)
Median	16.5	12.0	14.5	15.0	14.0
Range	10 - 23	9 - 19	9 - 22	12 - 17	9 - 23

Percentages are based on the total number of patients in the Randomized set.

Primary Objective Result(s)

Mean change in vitreous haze score in the study eye from baseline to last visit in core study (Full analysis set)

		Baseline					Change from Baseline				
Treatment	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**	**Mean**	**SD**	**Med**	**Min**	**Max**
AIN457 300mg q 2 weeks (N=8)	8	2.13	0.354	2.00	2.0	3.0	-1.00	1.035	-1.00	-3.0	0.0
AIN457 300mg q 4 weeks (N=10)	10	2.30	0.483	2.00	2.0	3.0	-1.35	0.580	-1.50	-2.0	0.0
AIN457 150mg q 4 weeks (N=8)	8	2.00	0.000	2.00	2.0	2.0	-0.88	0.835	-1.00	-2.0	0.0
Placebo q 2 weeks (N=4)	4	2.25	0.500	2.00	2.0	3.0	-1.13	0.250	-1.00	-1.5	-1.0

n is the number of patients with a value at both baseline and post baseline.
Med = Median. Min = minimum. Max = maximum.

Secondary Objective Result(s)

Change from baseline to last visit (LOCF) for composite immunosuppressive medication score in Core study (Full Analysis set)

		Baseline					Change from Baseline				
Treatment	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**	**Mean**	**SD**	**Med**	**Min**	**Max**
AIN457 300mg q 2 weeks (N=8)	8	2.46	3.096	2.00	0.0	9.7	-0.08	1.137	0.00	-2.0	2.0
AIN457 300mg q 4 weeks (N=10)	10	3.70	4.596	2.00	0.0	13.0	0.36	1.157	0.00	-2.0	2.0
AIN457 150mg q 4 weeks (N=8)	8	4.13	4.581	2.50	0.0	11.0	-0.23	1.674	0.00	-4.0	2.0
Placebo (N=4)	4	3.50	3.697	2.00	1.0	9.0	1.42	4.031	1.83	-3.0	5.0

n is the number of patients with a value at both baseline and post baseline.
Med = Median. Min = minimum. Max = maximum.

Safety Results

Adverse Events by System Organ Class

Incidence of AEs (any site) by primary system organ class (Safety set)

Primary system organ class	AIN457 300mg q 2 weeks N=8 n (%)	AIN457 300mg q 4 weeks N=10 n (%)	AIN457 150mg q 4 weeks N=8 n (%)	Placebo q 2 weeks N=4 n (%)	Total N=30 n (%)
Any primary system organ class	6 (75.0)	5 (50.0)	6 (75.0)	4 (100.0)	21 (70.0)
Cardiac disorders	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	1 (3.3)
Eye disorders	0 (0.0)	1 (10.0)	3 (37.5)	1 (25.0)	5 (16.7)
Gastrointestinal disorders	1 (12.5)	1 (10.0)	0 (0.0)	1 (25.0)	3 (10.0)
General disorders and administration site conditions	0 (0.0)	0 (0.0)	2 (25.0)	0 (0.0)	2 (6.7)
Immune system disorders	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)
Infections and infestations	2 (25.0)	1 (10.0)	0 (0.0)	0 (0.0)	3 (10.0)
Injury, poisoning and procedural complications	1 (12.5)	0 (0.0)	1 (12.5)	0 (0.0)	2 (6.7)
Investigations	0 (0.0)	1 (10.0)	0 (0.0)	2 (50.0)	3 (10.0)
Metabolism and nutrition disorders	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.3)
Musculoskeletal and connective tissue disorders	1 (12.5)	1 (10.0)	0 (0.0)	1 (25.0)	3 (10.0)
Nervous system disorders	1 (12.5)	0 (0.0)	1 (12.5)	0 (0.0)	2 (6.7)
Psychiatric disorders	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)
Respiratory, thoracic and mediastinal disorders	0 (0.0)	0 (0.0)	1 (12.5)	1 (25.0)	2 (6.7)
Skin and subcutaneous tissue disorders	1 (12.5)	0 (0.0)	1 (12.5)	0 (0.0)	2 (6.7)
Vascular disorders	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	1 (3.3)

- Primary system organ classes are presented alphabetically.

- A patient with multiple occurrences of an AE for a preferred term or system organ class under one treatment is counted only once in each specific category for that treatment.

Adverse Events by Preferred Term n (%)

All adverse events (any site), regardless of study drug relationship, by preferred term (Safety analysis set)

Preferred term	AIN457 300mg q 2 weeks N=8 n (%)	AIN457 300mg q 4 weeks N=10 n (%)	AIN457 150mg q 4 weeks N=8 n (%)	Placebo q 2 weeks N=4 n (%)	Total N=30 n (%)
-Total	6 (75.0)	5 (50.0)	6 (75.0)	4 (100.0)	21 (70.0)
Influenza	1 (12.5)	1 (10.0)	0 (0.0)	0 (0.0)	2 (6.7)
Blepharitis	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (3.3)
Cardiac arrest	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	1 (3.3)
Cataract	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.3)
Cataract nuclear	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.3)
Cataract traumatic	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.3)
Cough	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.3)
Dementia Alzheimer's type	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)
Dental caries	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (3.3)
Depression	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)
Diabetes mellitus	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.3)
Diarrhea	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	1 (3.3)
Epistaxis	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (3.3)
Erythema	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.3)
Eye injury	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.3)
GGT increased	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (3.3)
Gastroenteritis	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)
Glaucoma	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	1 (3.3)
Headache	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.3)
Hypertension	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	1 (3.3)
Intentional self-injury	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)
Intraocular pressure increased	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (3.3)
Joint swelling	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (3.3)
Lacrimation increased	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (3.3)
Nasopharyngitis	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)
Nausea	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)
Neck pain	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)
Ocular sarcoidosis	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.3)
Overdose	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)
Pain in extremity	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	1 (3.3)
Puncture site hemorrhage	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.3)
Pyrexia	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (3.3)
Rash	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)
Seasonal allergy	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)
Urinary tract infection	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)
Ventricular fibrillation	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	1 (3.3)
Weight increased	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	1 (3.3)
WBC count increased	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (3.3)

Preferred terms are sorted in descending order of the total column. A patient with multiple occurrences of an AE for a preferred term under one treatment is counted only once in each specific category for that treatment.
WBC = White blood cell

Serious Adverse Events and Deaths

Number (%) of patients who died, had serious adverse events, had adverse events, or had adverse events leading to discontinuation of study drug (Safety analysis set)

	AIN457 300 mg q 2 weeks N=8 n (%)	AIN457 300 mg q 4 weeks N=10 n (%)	AIN457 150 mg q 4 weeks N=8 n (%)	Placebo q 2 weeks N=4 n (%)	Total N=30 n (%)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
SAE	1 (12.5)	1 (10.0)	0 (0.0)	0 (0.0)	2 (6.7)
Ocular SAE of the study eye	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ocular SAE of the fellow eye	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Non-ocular SAE	1 (12.5)	1 (10.0)	0 (0.0)	0 (0.0)	2 (6.7)
SAE leading to discontinuation of study drug	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ocular AE of the study eye	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ocular AE of the fellow eye	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Non-ocular AE	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
AE	6 (75.0)	5 (50.0)	6 (75.0)	4 (100.0)	21 (70.0)
Ocular AE of the study eye	0 (0.0)	0 (0.0)	2 (25.0)	2 (50.0)	4 (13.3)
Ocular AE of the fellow eye	0 (0.0)	1 (10.0)	3 (37.5)	2 (50.0)	6 (20.0)
Non-ocular AE	6 (75.0)	5 (50.0)	4 (50.0)	2 (50.0)	17 (56.7)
AE leading to discontinuation of study drug	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ocular AE of the study eye	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ocular AE of the fellow eye	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Non-ocular AE	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

The categories are not mutually exclusive.

Serious adverse events (any site), regardless of study drug relationship, by primary system organ class and preferred term (Safety analysis set)

Patients with AE(s)	AIN457 300 mg q 2 weeks N=8 n (%)	AIN457 300 mg q 4 weeks N=10 n (%)	AIN457 150 mg q 4 weeks N=8 n (%)	Placebo q 2 weeks N=4 n (%)
Any System organ class	1 (12.5)	1 (10.0)	0 (0.0)	0 (0.0)
Cardiac disorders - total	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)
Cardiac arrest	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)
Ventricular fibrillation	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)
Injury, poisoning and procedural complications	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)
Overdose	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)

Primary system organ classes are presented alphabetically

Other Relevant Findings

None

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