Sponsor

Alcon Research, Ltd.

Generic Drug Name

Anecortave Acetate

Trial Indication(s)

Steroid induced intraocular pressure (IOP) elevation

Protocol Number

C-05-03

Protocol Title

A Study of the Safety and Efficacy of Anecortave Acetate for Treatment of Steroid Induced IOP Elevation

Clinical Trial Phase

Phase 2

Study Start/End Dates

19 December 2005 to 07 July 2009

Study Design/Methodology

This was a double-masked, randomized, multi-center, parallel group study with a placebo control.

Reason for Termination (if applicable)

Not Applicable

Centers

Subjects were recruited from 18 investigational sites located in the United States (12), Brazil (2), Mexico (1), the Netherlands (1), Italy (1), and Belgium (1).

Objectives

The primary objective of this study was to evaluate the safety and efficacy of Anecortave Acetate Depot (3, 15, or 30 mg) when administered by anterior juxtascleral depot (AJD) for treatment of elevated IOP following treatment with steroids.

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

Test Product: Anecortave Acetate 3 mg Depot (6mg/mL Anecortave Acetate Sterile Suspension)
Dose: 0.5 mL
Mode of Administration: anterior juxtascleral depot

Test Product: Anecortave Acetate 15 mg Depot (30mg/mL Anecortave Acetate Sterile Suspension)
Dose: 0.5 mL
Mode of Administration: anterior juxtascleral depot

Test Product: Anecortave Acetate 30 mg Depot (60mg/mL Anecortave Acetate Sterile Suspension)
Dose: 0.5 mL
Mode of Administration: anterior juxtascleral depot

Reference Product: Anecortave Acetate Vehicle
Dose: 0.5 mL
Mode of Administration: anterior juxtascleral depot

Statistical Methods

Analysis results presented for the intent-to-treat (ITT) data set, as the primary inference in the study, were based on the ITT data set.

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Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria:

- Either gender
- 18 years of age or older
- IOP elevation caused by steroid usage
- Other protocol-defined inclusion criteria may apply

Exclusion criteria:

- Under 18 years of age
- Other protocol-defined exclusion criteria may apply

Participant Flow Table

Patient Status
(All Patients Enrolled)

	Anecortave Acetate 3 mg	Anecortave Acetate 15 mg	Anecortave Acetate 30 mg	Anecortave Acetate Vehicle	Total
	N	N	N	N	N
Started	18	17	18	17	70
Completed	18	17	15	16	66
Discontinued	0	0	3	1	4
Reasons for Discontinuation					
Adverse Event	0	0	1	0	1
Lost to Follow-Up	0	0	2	1	3

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Baseline Characteristics

Demographic Statistics by Treatment Group
(Intent-to-Treat Data)

	Anecortave Acetate 3 mg	Anecortave Acetate 15 mg	Anecortave Acetate 30 mg	Anecortave Acetate Vehicle	Total
	N=18	N=17	N=18	N=17	N=70
Age					
18-64	13	14	11	12	50
65-74	2	2	6	3	13
75-84	2	1	1	2	6
85-94	1	0	0	0	1
Sex					
Male	10	9	10	11	40
Female	8	8	8	6	30

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Summary of Efficacy

Primary Outcome Measures

Comparison of Mean IOP Change from Baseline (mmHg) for the Study Eye
(Intent-to-Treat Data)
Anec Acet 3 mg versus Anec Acet Vehicle

	Screening	Combined	Week 1	Week 2	Week 4	Week 6	Month 3	Month 4.5	Exit Visit
Anec Acet 3 mg									
Mean	31.1	-3.0	-3.6	-3.2	-3.1	-2.6	-3.0	-2.6	-2.7
N	18	18	17	18	18	18	18	18	18
Anec Acet Vehicle									
Mean	34.1	-4.0	-4.0	-2.8	-3.4	-4.4	-4.6	-4.1	-4.8
N	17	17	15	17	17	17	17	17	17
Difference	-2.9	1.0	0.4	-0.4	0.3	1.8	1.6	1.5	2.0
P-value	0.3373	0.7278	0.9011	0.9029	0.9273	0.5847	0.6298	0.6475	0.5353
Upper 95% CI	3.1	7.0	7.0	6.1	6.8	8.3	8.1	8.0	8.5
Lower 95% CI	-9.0	-4.9	-6.1	-6.9	-6.2	-4.7	-4.9	-5.0	-4.4

Anec Acet = Anecortave Acetate; CI = Confidence interval
Combined = Results pooled across Week 1, Week 2, Week 4, Week 6, Month 3, Month 4.5 and Exit Visit
Estimates based upon least squares means using repeated measures analysis of variance. Baseline estimates obtained from separate model.

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Comparison of Mean IOP Change from Baseline (mmHg) for the Study Eye
(Intent-to-Treat Data)
Anec Acet 15 mg versus Anec Acet Vehicle

	Screening	Combined	Week 1	Week 2	Week 4	Week 6	Month 3	Month 4.5	Exit Visit
Anec Acet 15 mg									
Mean	37.6	-9.2	-4.1	-5.4	-11.5	-12.2	-11.4	-10.2	-9.8
N	17	17	17	17	17	17	17	17	17
Anec Acet Vehicle									
Mean	34.1	-4.0	-4.0	-2.8	-3.4	-4.4	-4.6	-4.1	-4.8
N	17	17	15	17	17	17	17	17	17
Difference	3.6	-5.2	-0.0	-2.6	-8.1	-7.8	-6.8	-6.1	-5.0
P-value	0.2502	0.0878	0.9897	0.4284	0.0162	0.0205	0.0416	0.0677	0.1350
Upper 95% CI	9.8	0.8	6.6	3.9	-1.5	-1.2	-0.3	0.4	1.6
Lower 95% CI	-2.6	-11.2	-6.7	-9.2	-14.6	-14.3	-13.4	-12.7	-11.6

Anec Acet = Anecortave Acetate; CI = Confidence interval
Combined = Results pooled across Week 1, Week 2, Week 4, Week 6, Month 3, Month 4.5 and Exit Visit
Estimates based upon least squares means using repeated measures analysis of variance. Baseline estimates obtained from separate model.

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Comparison of Mean IOP Change from Baseline (mmHg) for the Study Eye
(Intent-to-Treat Data)
Anec Acet 30 mg versus Anec Acet Vehicle

	Screening	Combined	Week 1	Week 2	Week 4	Week 6	Month 3	Month 4.5	Exit Visit
Anec Acet 30 mg									
Mean	32.9	-5.2	-4.2	-3.6	-5.4	-5.8	-5.8	-5.6	-5.9
N	18	18	18	18	18	18	18	18	18
Anec Acet Vehicle									
Mean	34.1	-4.0	-4.0	-2.8	-3.4	-4.4	-4.6	-4.1	-4.8
N	17	17	15	17	17	17	17	17	17
Difference	-1.1	-1.2	-0.2	-0.8	-2.0	-1.4	-1.2	-1.4	-1.1
P-value	0.7160	0.6937	0.9504	0.7972	0.5485	0.6784	0.7055	0.6625	0.7329
Upper 95% CI	5.0	4.7	6.3	5.6	4.5	5.1	5.2	5.0	5.3
Lower 95% CI	-7.2	-7.1	-6.7	-7.3	-8.4	-7.8	-7.7	-7.9	-7.6

Anec Acet = Anecortave Acetate; CI = Confidence interval
Combined = Results pooled across Week 1, Week 2, Week 4, Week 6, Month 3, Month 4.5 and Exit Visit
Estimates based upon least squares means using repeated measures analysis of variance. Baseline estimates obtained from separate model.

Secondary Outcome Measures

None reported.

Summary of Safety

The evaluation of safety was conducted in patients who were randomized into the study and received a single unilateral administration of test article by an anterior juxtascleral depot (AJD) procedure (safety analysis set). No deaths or serious adverse drug reactions (treatment-related serious adverse events) were reported during the study. Twelve patients experienced serious adverse events assessed as unrelated to the use of test article or the AJD procedure, and one experienced an AE causing discontinuation. Review of the nonserious adverse event that resulted in the patient discontinuing from the study revealed no safety issues.

Safety Results

Frequency and Incidence of Adverse Events Related to Test Article (Safety Analysis Set)

Coded Adverse Event	AA 30 mg N = 18		AA 15 mg N=17		AA 3 mg N = 18		Vehicle N = 17	
	N	%	N	%	N	%	N	%
Cataract	1	5.6	1	5.9	0	0.0	0	0.0
Keratitis	1	5.6	0	0.0	0	0.0	0	0.0

Coded Adverse Events = MedDRA Preferred Term (version 11.0) presented by System Organ
AA 30 mg = 0.5 mL of 60 mg/ml Anecortave Acetate Suspension
AA 15 mg = 0.5 mL of 30 mg/ml Anecortave Acetate Suspension
AA 3 mg = 0.5 mL of 6 mg/ml Anecortave Acetate Suspension
Vehicle = 0.5 mL of Anecortave Acetate Vehicle

Frequency and Incidence of Adverse Events Related to the AJD Procedure (Safety Analysis Set)

Coded Adverse Event	AA 30 mg N = 18		AA 15 mg N=17		AA 3 mg N = 18		Vehicle N = 17	
	N	%	N	%	N	%	N	
Conjunctival haemorrhage	1	5.6	2	11.8	2	11.1	1	5.9
Eye pain	2	11.1	3	17.6	0	0.0	1	5.9
Ocular hyperemia	0	0.0	0	0.0	1	5.6	1	5.9
Ocular discomfort	0	0.0	1	5.9	1	5.6	0	0.0
Blurred vision	1	5.6	0	0.0	0	0.0	0	0.0
Iritis	1	5.6	0	0.0	0	0.0	0	0.0

Coded Adverse Events = MedDRA Preferred Term (version 11.0) presented by System Organ
AA 30 mg = 0.5 mL of 60 mg/ml Anecortave Acetate Suspension
AA 15 mg = 0.5 mL of 30 mg/ml Anecortave Acetate Suspension
AA 3 mg = 0.5 mL of 6 mg/ml Anecortave Acetate Suspension
Vehicle = 0.5 mL of Anecortave Acetate Vehicle

Other Relevant Findings

No other relevant findings to disclose.

Date of Clinical Trial Report

30 April 2010