ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 11/02/2012

ClinicalTrials.gov ID: NCT00884585

Study Identification

Unique Protocol ID:	192371-016
Brief Title:	Efficacy and Safety Study of Cyclosporine 0.010% to Treat Atopic Keratoconjunctivitis
Official Title:	
Secondary IDs:	

Study Status

Record Verification:	November 2012
Overall Status:	Completed
Study Start:	May 2009
Primary Completion:	October 2010 [Actual]
Study Completion:	July 2011 [Actual]

Sponsor/Collaborators

Sponsor:	Allergan
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No

IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 32,133 Serial Number: 0189 Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	This study evaluates the efficacy and safety of Cyclosporine 0.010% eye drops in the treatment of Atopic Keratoconjunctivitis (chronic and severe inflammation of the eye). The study consists of a double-masked phase, and open-labeled phase, and an open-labeled maintenance phase. For the first 3 months of the study, patients will receive either masked Cyclosporine 0.010% eye drops or vehicle four times daily; for the next 6 months, patients may receive open-labeled Cyclosporine 0.010% eye drops four times daily. At month 9, patients who are in remission, will be re-randomized to receive either open-labeled Cyclosporine 0.010% eye drops four times daily or twice daily.
Detailed Description:	

Conditions

Conditions:	Atopic Conjunctivitis
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	2

Masking:	Double Blind (Subject, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	176 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Cyclosporine Ophthalmic Solution (COS) followed by COS Cyclosporine ophthalmic solution 0.010% administered 4 times a day to the qualified eye(s) for up to 12 months; at Month 9 the dose may be adjusted to 2 times a day.	Drug: Cyclosporine 0.010% Cyclosporine ophthalmic solution 0.010% administered 4 times a day to the qualified eye(s) for up to 12 months; at Month 9 the dose may be adjusted to 2 times a day.
Placebo followed by COS Placebo (cyclosporine vehicle) administered 4 times a day to the qualified eye(s) for 3 months followed by cyclosporine ophthalmic solution 0.010% up to 9 additional months; at Month 9 the dose may be adjusted to 2 times a day.	Drug: Cyclosporine Vehicle Placebo (cyclosporine vehicle) administered 4 times a day to the qualified eye(s) for 3 months. Drug: Cyclosporine 0.010% Cyclosporine ophthalmic solution 0.010% administered 4 times a day to the qualified eye(s) for up to 12 months; at Month 9 the dose may be adjusted to 2 times a day.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	12 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- Have a clinical diagnosis of Atopic Keratoconjunctivitis (chronic and severe inflammation of the eye)
- Be on stable doses of your current AKC medications for at least 2 weeks

Exclusion Criteria:

- You have used contact lenses within 48 hours of Day 1 or think you may have to wear contact lenses during the study
- You are pregnant, breastfeeding, or planning to become pregnant during the study

- You have used a calcineurin inhibitors (e.g. topical tacrolimus or topical pimecrolimus) on or around your eyes including eyelids within 4 weeks

Contacts/Locations

Study Officials: Medical Director
Study Director
Allergan, Inc.

Locations: United States, California
Bakersfield, California, United States

Canada, Ontario
Ottawa, Ontario, Canada

Australia, New South Wales
Randwick, New South Wales, Australia

Germany
Munich, Bavaria, Germany

Spain
Valladolid, Spain

France
Dijon, Burgundy, France

United Kingdom
Newcastle-upon-tyne, Tyne and Wear, United Kingdom

New Zealand
Wellington, New Zealand

India
Bangalore, Karnataka, India

Czech Republic
Prague, Czech Republic

Israel
Tel Aviv, Israel

Italy
Rome, Italy

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Pre-Assignment Details	Per protocol defined pre-specified criteria, both eyes could qualify for treatment. However, only one eye was designated as the study eye.

Reporting Groups

	Description
Cyclosporine Ophthalmic Solution (COS) Followed by COS	Cyclosporine ophthalmic solution 0.010% administered 4 times a day to the qualified eye(s) for up to 12 months; at Month 9 the dose may be adjusted to 2 times a day.
Placebo Followed by COS	Placebo (cyclosporine vehicle) administered 4 times a day to the qualified eye(s) for 3 months followed by cyclosporine ophthalmic solution 0.010% up to 9 additional months; at Month 9 the dose may be adjusted to 2 times a day.

Double-Masked Phase (Day 1-Month 3)

	Cyclosporine Ophthalmic Solution (COS) Followed by COS	Placebo Followed by COS
Started	89	87
Completed	79	83 [1]
Not Completed	10	4

[1] All placebo patients who completed the double-masked phase received COS in the open-label phase.

Open-Label Phase (Months 3-9)

	Cyclosporine Ophthalmic Solution (COS) Followed by COS	Placebo Followed by COS
Started	162 [1]	0 [2]
Completed	147	0
Not Completed	15	0

[1] All patients who completed the double-masked phase received COS in the open-label phase.
[2] All placebo patients who completed the double-masked phase received COS in the open-label phase.

Open-Label Maintenance (Months 9-12)

	Cyclosporine Ophthalmic Solution (COS) Followed by COS	Placebo Followed by COS
Started	147	0
Completed	144	0
Not Completed	3	0

Baseline Characteristics

Reporting Groups

	Description
Cyclosporine Ophthalmic Solution (COS) Followed by COS	Cyclosporine ophthalmic solution 0.010% administered 4 times a day to the qualified eye(s) for up to 12 months; at Month 9 the dose may be adjusted to 2 times a day.
Placebo Followed by COS	Placebo (cyclosporine vehicle) administered 4 times a day to the qualified eye(s) for 3 months followed by cyclosporine ophthalmic solution 0.010% up to 9 additional months; at Month 9 the dose may be adjusted to 2 times a day.

Baseline Measures

	Cyclosporine Ophthalmic Solution (COS) Followed by COS	Placebo Followed by COS	Total
Number of Participants	89	87	176
Age, Customized [units: Participants]			
<18 years	7	8	15
18 to <30 years	15	13	28

	Cyclosporine Ophthalmic Solution (COS) Followed by COS	Placebo Followed by COS	Total
30 to <50 years	32	38	70
50 to <65 years	27	22	49
>=65 years	8	6	14
Gender, Male/Female [units: Participants]			
Female	46	39	85
Male	43	48	91

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Treatment Responders
Measure Description	Treatment responders are defined as patients with a ≥ 1 grade improvement from baseline in punctate corneal staining score and a ≥ 4 grade improvement from baseline in composite symptom score in the study eye. The punctate corneal staining score is assessed on a scale of 0 to 5 (0 is ≤2 dots and 5 is >316 dots (approximately) or ulcer/erosion). The composite symptom score is based on 5 symptoms (itching, tearing, ocular discomfort, photophobia, mucous discharge). The composite symptom score (0 to 15) is the sum of 5 symptoms (each symptom is assessed on a scale of 0=absent to 3=severe).
Time Frame	Baseline, Month 2
Safety Issue?	No

Analysis Population Description

Intent to Treat: all randomized patients

Reporting Groups

	Description
Cyclosporine Ophthalmic Solution (COS) Followed by COS	Cyclosporine ophthalmic solution 0.010% administered 4 times a day to the qualified eye(s) for up to 12 months; at Month 9 the dose may be adjusted to 2 times a day.
Placebo	Placebo (cyclosporine vehicle) administered 4 times a day to the qualified eye(s) for 3 months.

Measured Values

	Cyclosporine Ophthalmic Solution (COS) Followed by COS	Placebo
Number of Participants Analyzed	89	87
Percentage of Treatment Responders [units: Percentage of Patients]	21.3	17.2

2. Secondary Outcome Measure:

Measure Title	Percentage of Punctate Corneal Staining Responders
Measure Description	Punctate corneal staining responders defined as patients achieving a punctate corneal staining score of 0 or 1 in the study eye. Punctate corneal staining is assessed on a scale of 0 to 5 where 0 is ≤2 dots, 1 is >2 dots but ≤ 10 dots, 2 is > 10 dots but ≤ 32 dots, 3 is > 32 dots but ≤ 100 dots (approximately), 4 is > 100 dots (approximately) but ≤ 316 dots (approximately), and 5 is >316 dots (approximately) or ulcer/erosion.
Time Frame	Month 2
Safety Issue?	No

Analysis Population Description

Intent to Treat: all randomized patients

Reporting Groups

	Description
Cyclosporine Ophthalmic Solution (COS) Followed by COS	Cyclosporine ophthalmic solution 0.010% administered 4 times a day to the qualified eye(s) for up to 12 months; at Month 9 the dose may be adjusted to 2 times a day.
Placebo	Placebo (cyclosporine vehicle) administered 4 times a day to the qualified eye(s) for 3 months.

Measured Values

	Cyclosporine Ophthalmic Solution (COS) Followed by COS	Placebo
Number of Participants Analyzed	89	87
Percentage of Punctate Corneal Staining Responders [units: Percentage of Patients]	24.7	23.0

3. Secondary Outcome Measure:

Measure Title	Percentage of Patients With an Improvement in the Composite Symptom Score
Measure Description	Composite symptom score improvement is defined as a 4 or more grade decrease from baseline in composite symptom score in the study eye. The composite symptom score is based on 5 symptoms (itching, tearing, ocular discomfort, photophobia, mucous discharge). Each of the 5 symptoms is assessed on a scale of 0=absent to 3=severe. The composite symptom score is the sum of all 5 individual symptom scores, where 0 is no symptoms and 15 is the most severe symptoms.
Time Frame	Baseline, Month 2
Safety Issue?	No

Analysis Population Description

Intent to Treat: all randomized patients

Reporting Groups

	Description
Cyclosporine Ophthalmic Solution (COS) Followed by COS	Cyclosporine ophthalmic solution 0.010% administered 4 times a day to the qualified eye(s) for up to 12 months; at Month 9 the dose may be adjusted to 2 times a day.
Placebo	Placebo (cyclosporine vehicle) administered 4 times a day to the qualified eye(s) for 3 months.

Measured Values

	Cyclosporine Ophthalmic Solution (COS) Followed by COS	Placebo
Number of Participants Analyzed	89	87
Percentage of Patients With an Improvement in the Composite Symptom Score [units: Percentage of Patients]	30.3	28.7

4. Secondary Outcome Measure:

Measure Title	Percentage of Patients With an Improvement in the Punctate Corneal Staining Score
Measure Description	Punctate corneal staining improvement is defined as a 1 or more grade decrease from baseline in the study eye. The punctate corneal staining score is assessed on a scale of 0 to 5 where 0 is ≤2 dots, 1 is >2 dots but ≤ 10 dots, 2 is > 10 dots but ≤ 32 dots, 3 is > 32 dots but ≤ 100 dots (approximately), 4 is > 100 dots (approximately) but ≤ 316 dots (approximately), and 5 is >316 dots (approximately) or ulcer/erosion.
Time Frame	Baseline, Month 2

Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Cyclosporine Ophthalmic Solution (COS) Followed by COS	Cyclosporine ophthalmic solution 0.010% administered 4 times a day to the qualified eye(s) for up to 12 months; at Month 9 the dose may be adjusted to 2 times a day.
Placebo	Placebo (cyclosporine vehicle) administered 4 times a day to the qualified eye(s) for 3 months.

Measured Values

	Cyclosporine Ophthalmic Solution (COS) Followed by COS	Placebo
Number of Participants Analyzed	89	87
Percentage of Patients With an Improvement in the Punctate Corneal Staining Score [units: Percentage of Patients]	42.7	42.5

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	The Safety Population was used for all adverse event (AE)/serious adverse event (SAE) reporting. All patients in the safety population received at least 1 dose of study medication.

Reporting Groups

	Description
Cyclosporine Ophthalmic Solution (COS) Followed by COS	Cyclosporine ophthalmic solution 0.010% administered 4 times a day to the qualified eye(s) for up to 12 months; at Month 9 the dose may be adjusted to 2 times a day.
Placebo	Placebo (cyclosporine vehicle) administered 4 times a day to the qualified eye(s) for 3 months.

Serious Adverse Events

	Cyclosporine Ophthalmic Solution (COS) Followed by COS	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	11/171 (6.43%)	3/87 (3.45%)
Gastrointestinal disorders		
Abdominal Hernia [A] †	1/171 (0.58%)	0/87 (0%)
Immune system disorders		
Anaphylactic Shock [A] †	0/171 (0%)	1/87 (1.15%)
Infections and infestations		
Herpes Zoster [A] *	1/171 (0.58%)	0/87 (0%)
Infectious Mononucleosis [A] †	1/171 (0.58%)	0/87 (0%)
Pneumonia [A] †	1/171 (0.58%)	0/87 (0%)
Injury, poisoning and procedural complications		
Forearm Fracture [A] †	1/171 (0.58%)	0/87 (0%)
Joint Injury [A] *	1/171 (0.58%)	0/87 (0%)
Investigations		
Prostatic Specific Antigen Increased [A] †	1/171 (0.58%)	0/87 (0%)
Musculoskeletal and connective tissue disorders		
Osteoarthritis [A] *	1/171 (0.58%)	0/87 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Breast Cancer [A] †	0/171 (0%)	1/87 (1.15%)
Psychiatric disorders		
Depression [A] *	1/171 (0.58%)	0/87 (0%)
Respiratory, thoracic and mediastinal disorders		
Epistaxis [A] †	0/171 (0%)	1/87 (1.15%)
Skin and subcutaneous tissue disorders		

	Cyclosporine Ophthalmic Solution (COS) Followed by COS	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Dermatitis Atopic [A] *	1/171 (0.58%)	0/87 (0%)
Vascular disorders		
Hypertension [A] †	1/171 (0.58%)	0/87 (0%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA version 10.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Cyclosporine Ophthalmic Solution (COS) Followed by COS	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	44/171 (25.73%)	16/87 (18.39%)
Eye disorders		
Allergic Keratitis [A] †	24/171 (14.04%)	10/87 (11.49%)
Blepharitis [A] †	10/171 (5.85%)	3/87 (3.45%)
Punctate Keratitis [A] †	10/171 (5.85%)	3/87 (3.45%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA version 10.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

A disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 90 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Results Point of Contact:

Name/Official Title: Therapeutic Area Head,
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