Efficacy and Safety of an Intracanalicular Dexamethasone Insert (0.4 mg) for the Treatment of Allergic Conjunctivitis

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American Academy of Ophthalmology Annual Meeting | November 12-15, 2021 | New Orleans, LA

Disclosures

- Steven M. Silverstein, Kenneth R. Kenyon KR, Eugene B. McLaurin EB, and Michelle A. Sato were investigators in the clinical trials
- Erin Reilly, Matthew Cheung, Michael H. Goldstein are employees of Ocular Therapeutix, Inc.
- The clinical trials were sponsored by Ocular Therapeutix, Inc.

Background

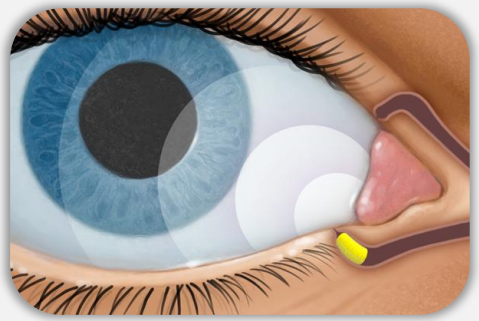
Allergic conjunctivitis (AC) affects up to 40% of the US population and can negatively impact patients' quality of life[1-3], but existing topical therapies:

- Require multiple daily instillations to maintain symptomatic relief[4,5]
- Contain BAK which can cause discomfort and corneal cytotoxicity[6]
- Require close supervision to avoid patient overuse and misuse[5,7]

Other treatment approaches that address these key limitations are needed

DEXTENZA (dexamethasone ophthalmic insert) 0.4 mg

- Intracanalicular insert with dexamethasone in a polyethylene glycol (PEG) hydrogel that delivers therapy for up to 30 days[8]
  - Preservative-free
  - Fully resorbable
  - Conjugated with fluorescein for visualization



Rendering of insert placed in the canaliculus

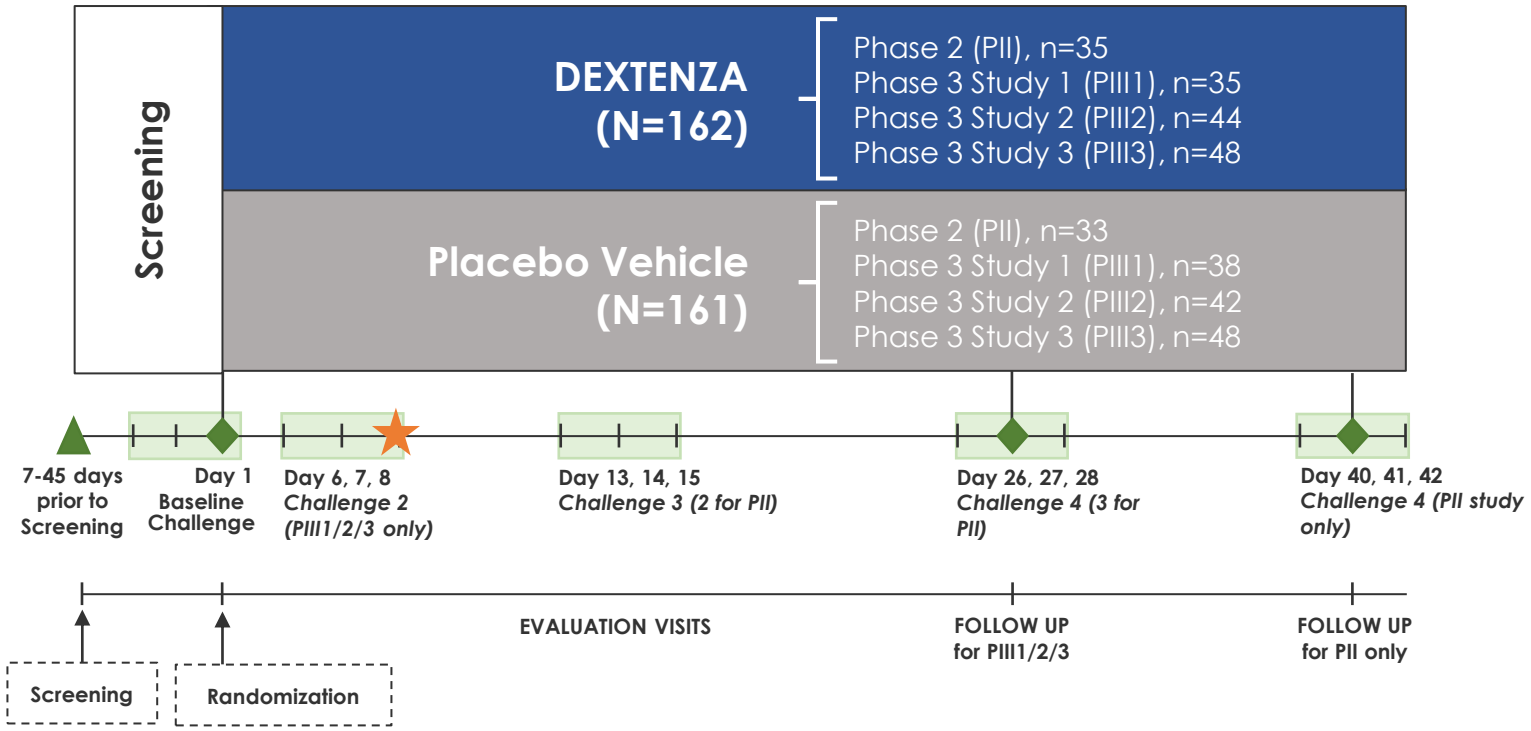
- Physician-administered and designed to obviate the need for corticosteroid drops[9]
- FDA-approved for the treatment of ocular itching associated with allergic conjunctivitis, and ocular inflammation and pain following ophthalmic surgery[8]

References: 1. Rosario N, et al. *Curr Opin Allergy Clin Immunol*. 2011;11(5):471–476. **2.** Singh K, et al. *J Allergy Clin Immunol*. 2010;126:778-783. **3.** Meltzer EO, et al. *Allergy Asthma Proc*. 2009;30(3):244-254. **4.** American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern Guidelines: Conjunctivitis. American Academy of Ophthalmology. Available at https://www.aaojournal.org/article/S0161-6420(18)32646-0/fulltext. Accessed October 18, 2021. **5.** Dupuis P, et al. *Allergy Asthma Clin Immunol*. 2020;16:5. **6.** Goldstein MH, et al. *Eye (Lond)*. 2021:1–8. **7.** Phulke S, et al. *J Curr Glaucoma Pract*. 2017;11(2):67-72. **8.** DEXTENZA [package insert]. Bedford, MA: Ocular Therapeutix, Inc; 2021. **9.** Sawhney AS, Jarrett P, Bassett M, Blizzard C, inventors; Incept, LLC, assignee. Drug delivery through hydrogel plugs. US patent 8,409,606 B2. April 2, 2013.

BAK, benzalkonium chloride

Pooled Analysis of Four DEXTENZA Clinical Trials

- **One Phase 2** (PII) and **three Phase 3** (PIII-1, PIII-2, PIII-3) clinical trials using a modified Ora-CAC® (Conjunctival Allergen Challenge) Model
  - Randomized, double-masked, vehicle-controlled studies in allergic conjunctivitis subjects
- Efficacy analysis included three Phase 3 studies and safety analysis included all four studies



Key Inclusion Criteria

- History of allergic conjunctivitis
- Positive skin test to seasonal and/or perennial allergens
- Bilateral CAC reaction

Key Endpoints

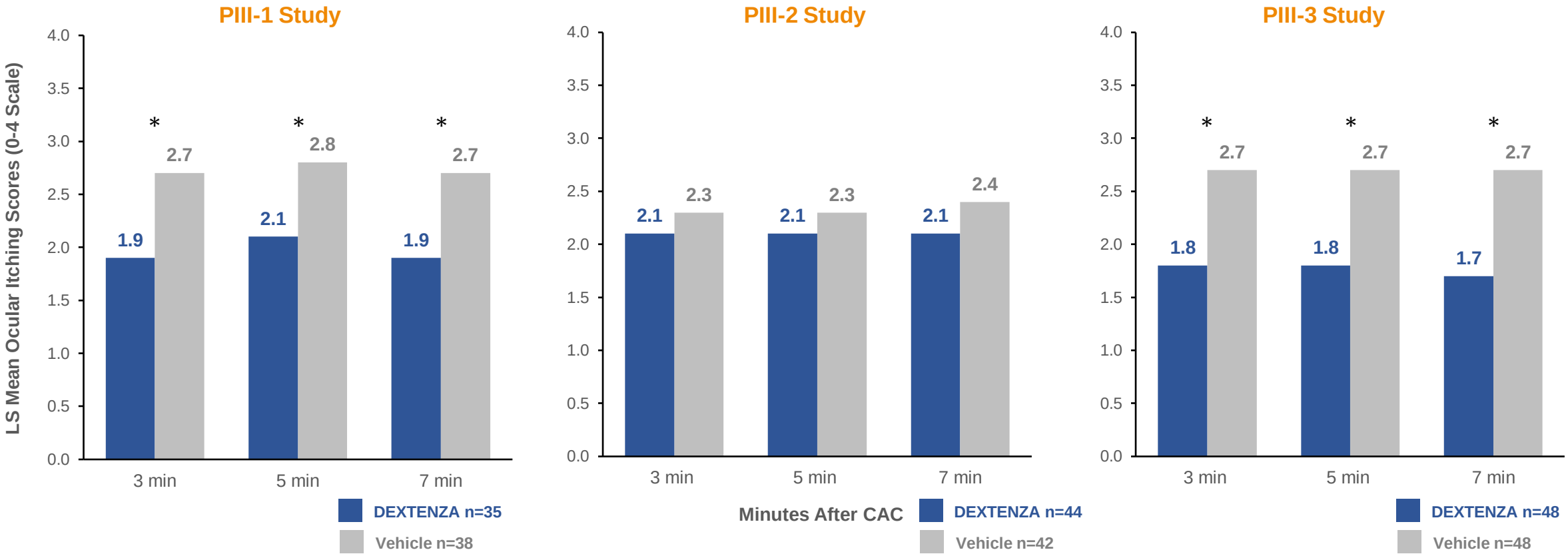
- Ocular Itching 3, 5 and 7 minutes post-CAC on Day 8
- Conjunctival redness 7, 15 and 20 minutes post-CAC on Day 8

Primary Endpoint

Series of 4 CAC Challenges

Ocular Itching on Day 8 by Phase 3 Study

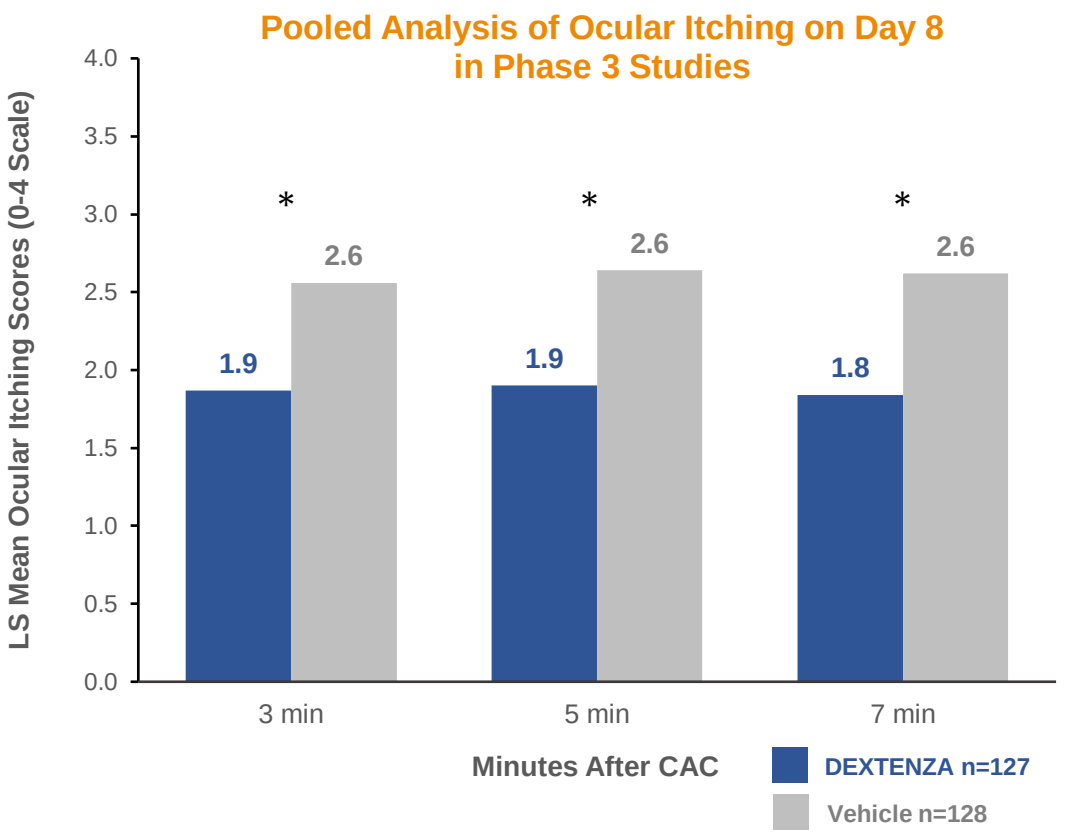
- DEXTENZA statistically significantly reduced mean ocular itching scores compared to vehicle in two Phase 3 studies (P<0.05)

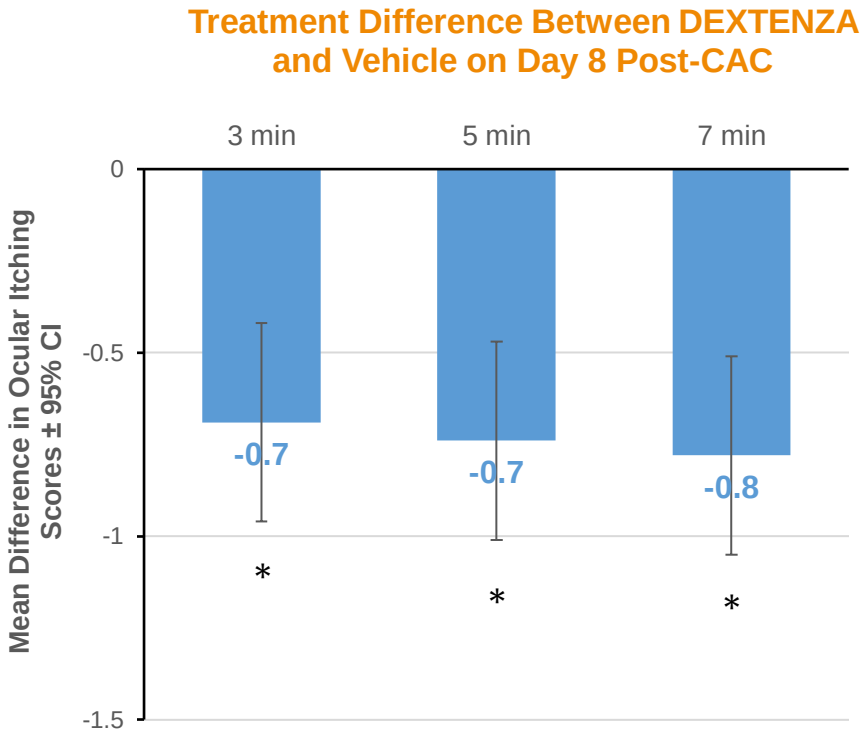


*Statistically significant difference; P<0.05
Reference: DEXTENZA [package insert]
CAC, conjunctival allergen challenge; LS, least square

Pooled Analysis of Ocular Itching

- DEXTENZA achieved statistically significant lower mean ocular itching scores at all 3 post-CAC timepoints on Day 8 (P<0.0001)

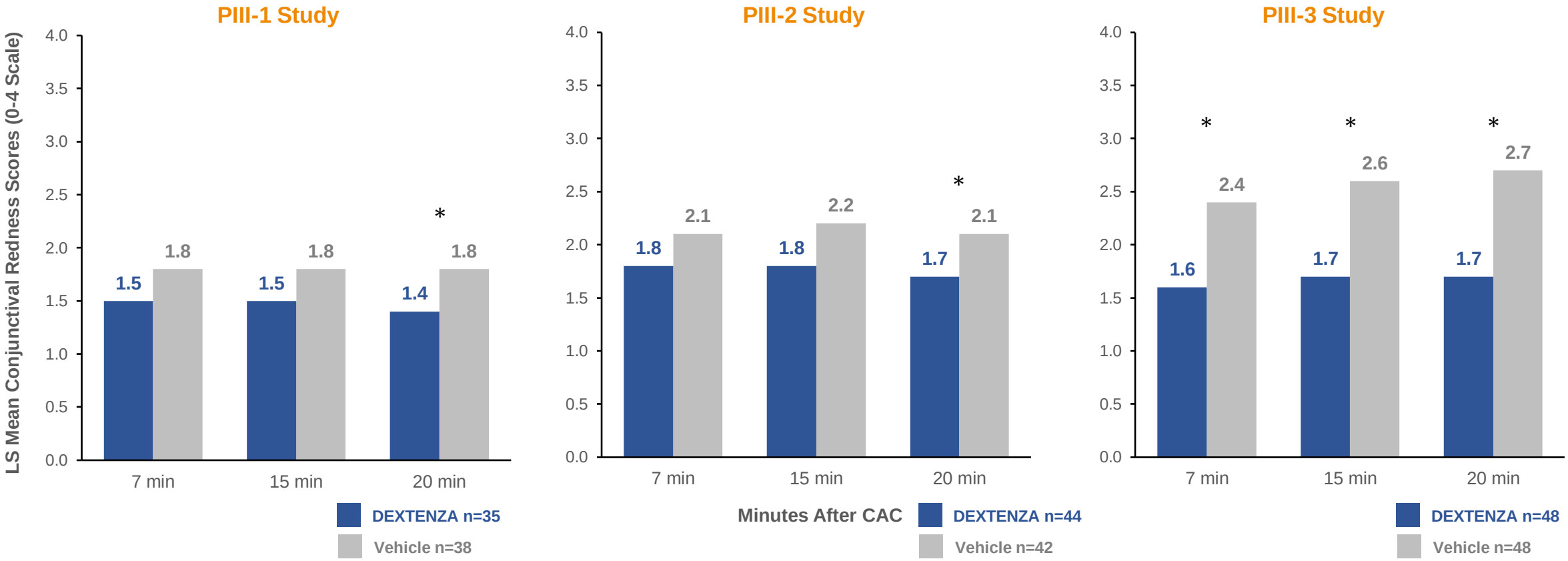




* Statistically significant difference; P<0.0001
Analysis population: Intent-to-treat with observed data
CAC, conjunctival allergen challenge; CI, confidence interval; LS, least square

Conjunctival Redness on Day 8 by Phase 3 Study

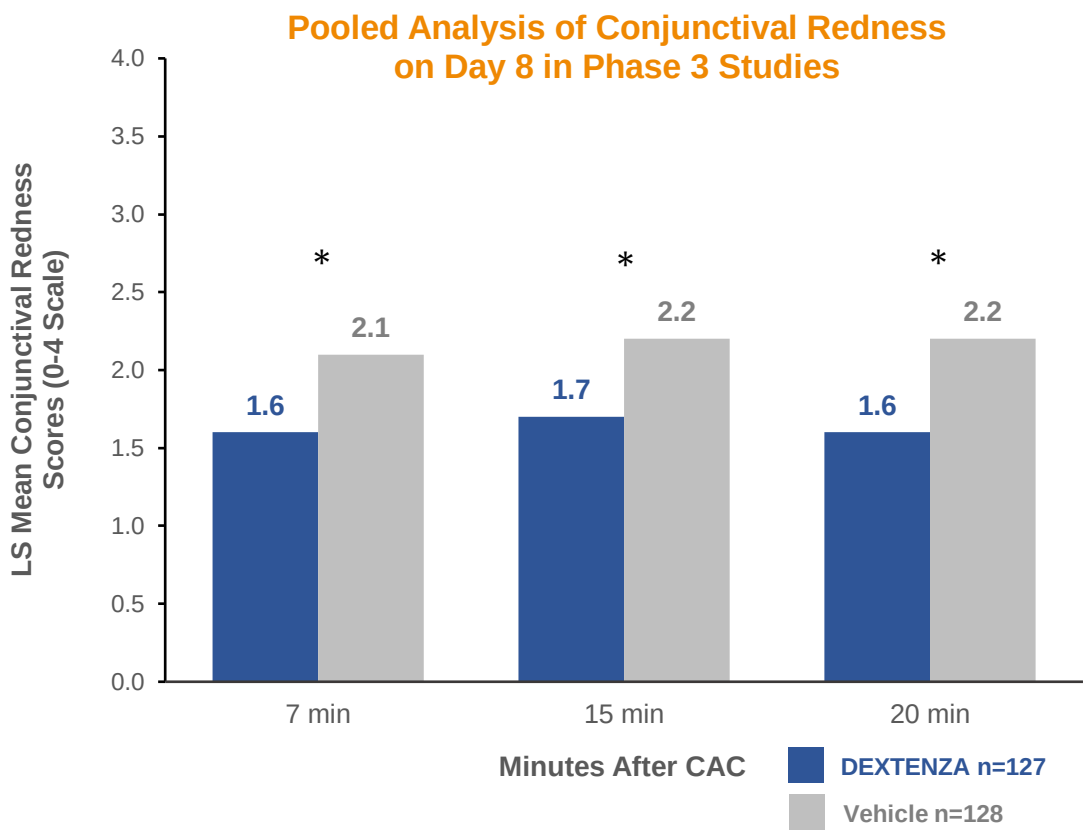
- Study 3 demonstrated significant differences in conjunctival redness scores in favor of DEXTENZA on Day 8 (P<0.05)

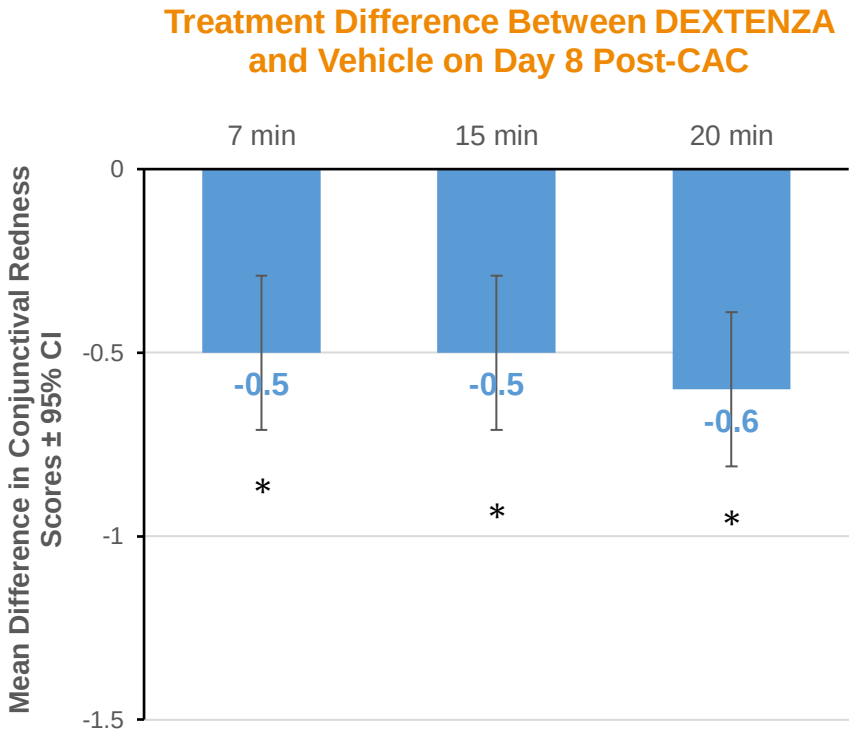


*Statistically significant difference; P<0.05
Analysis population: Intent-to-treat with observed data
CAC, conjunctival allergen challenge; LS, least square

Pooled Analysis of Conjunctival Redness

- DEXTENZA significantly lowered mean conjunctival redness scores at all 3 post-CAC timepoints on Day 8 (P<0.0001)





* Statistically significant difference; P<0.0001
Analysis population: Intent-to-treat with observed data
CAC, conjunctival allergen challenge; CI, confidence interval; LS, least square

DEXTENZA Safety Summary

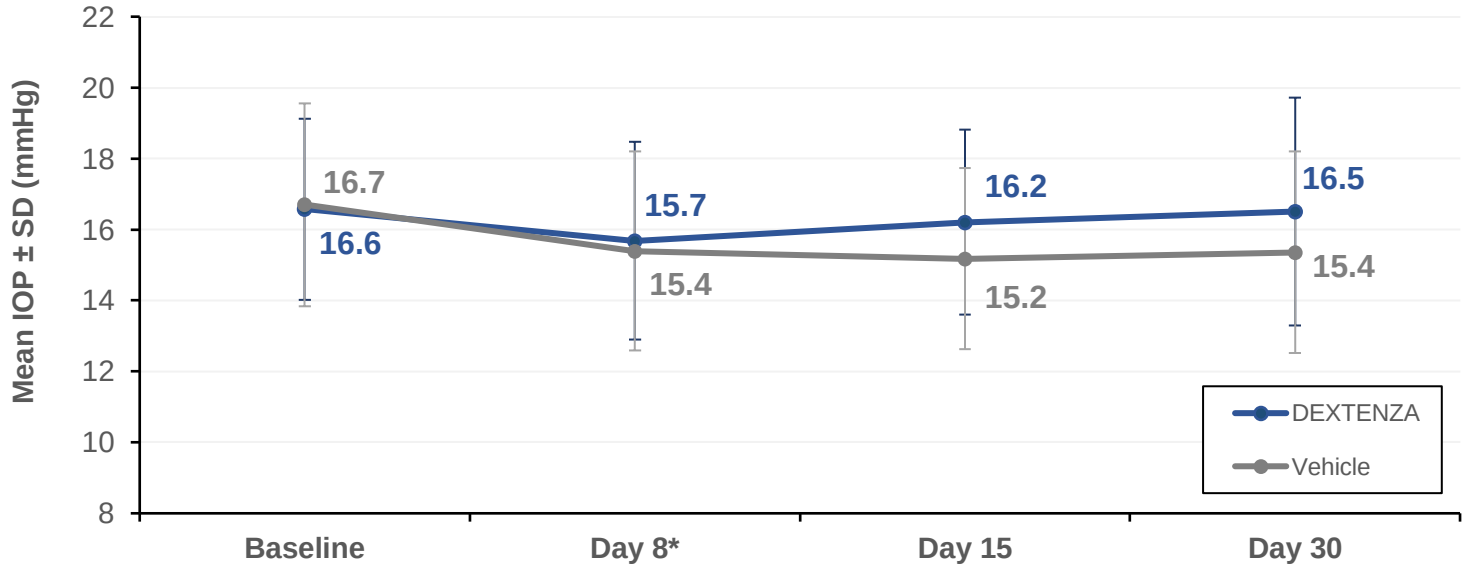
- No severe AEs were reported
  - All were mild or moderate in severity
- No ocular serious AEs were reported
- No dacryocanaliculitis AEs reported in the DEXTENZA group
- One non-ocular serious AE deemed unrelated to treatment was observed in the DEXTENZA group
  - Hospitalization due to depression
- Lower proportion of the DEXTENZA group reported an AE compared to the vehicle group (18.8% vs 24.2%)

Most Common Adverse Events Reported in the DEXTENZA Group

Adverse Event	DEXTENZA N=154 n (%)	Vehicle N=161 n (%)
Increased intraocular pressure	5 (3.2)	0
Reduced visual acuity	2 (1.3)	0
Increased lacrimation	2 (1.3)	6 (3.7)
Eye discharge	2 (1.3)	4 (2.5)

Intraocular Pressure Elevation with DEXTENZA

Mean IOP Levels



	Baseline	Day 8*	Day 15	Day 30
DEXTENZA†	n=308 eyes	n=232 eyes	n=276 eyes	n=294 eyes
Vehicle†	n=322 eyes	n=238 eyes	n=292 eyes	n=302 eyes

Management of Increased IOP in DEXTENZA Subjects

Increased IOP	DEXTENZA N=154
Total Number of Subjects	5
Management	
No action	1
Removal of DEXTENZA	0
Topical Medication Therapy	4

* PIII1, PIII2, and PIII3 Study only. PII Study did not have a Day 8 visit.
† Safety population. DEXTENZA N=154 subjects and Placebo N=161. Subjects received DEXTENZA or placebo vehicle insert bilaterally.
IOP, intraocular pressure; SD, standard deviation

Conclusions

- DEXTENZA for the treatment of allergic conjunctivitis was evaluated in **four vehicle-controlled clinical trials with 315 subjects** using the modified CAC model with multiple repeated challenges
- DEXTENZA statistically significantly reduced ocular itching at 3, 5, and 7 min post-CAC on Day 8 in two Phase 3 studies and conjunctival redness at 7, 15, and 20 min post-CAC on Day 8 in one Phase 3 study
- Pooled analysis of three Phase 3 studies demonstrated **DEXTENZA statistically significantly reduced ocular itching and conjunctival redness** compared to placebo vehicle at all timepoints on Day 8
- DEXTENZA was generally **well tolerated with a favorable safety profile** and no serious ocular adverse events reported across four studies