# Pooled Analysis Evaluating Efficacy and Safety of an Intracanalicular Dexamethasone Insert for the Treatment of Allergic Conjunctivitis

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# FINANCIAL DISCLOSURES

Rubin JM, Silverstein SM, Kenyon KR, McLaurin EB, Evans DG, and Sato MA were investigators in the clinical trial.

Reilly E, Cheung M, Vantipalli S, Metzinger JL, Goldstein MH are employees of Ocular Therapeutix, Inc.

Clinical Trial Sponsor: Ocular Therapeutix, Inc.

# Background and Rationale

## Allergic Conjunctivitis Treatment

Allergic conjunctivitis (AC) is a **prevalent**, **allergen-induced**, **inflammatory-mediated** eye disorder that places a burden on patients and healthcare practices.[1,2]

Current topical drop therapies have limitations including potential for **noncompliance**, and **preservatives toxicity**.[3,4]

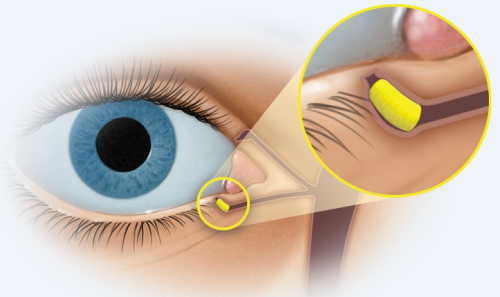
Although topical ophthalmic steroids are effective in treating allergic conjunctivitis, **physicians report infrequent use due to side effects and risk of abuse** associated with long-term use.[5,6]

## DEXTENZA (dexamethasone ophthalmic insert) 0.4mg

DEXTENZA is a physician-administered, hydrogel-based, intracanalicular insert designed to obviate the need for corticosteroid drops.[7]

### Product Attributes[7,8]

- Contains 0.4mg dexamethasone in a polyethylene glycol (PEG) hydrogel
- Designed to provide effective tapered therapy for up to 30 days with a single insert
- Alternative to conventional steroid eye drops
- Preservative-free
- Fully biodegradable
- Conjugated with fluorescein for visualization



*Rendering of placement of insert in the canaliculus*

**References: 1**. Leonardi A, et al. *Curr Opin Allergy Clin Immunol*. 2015;15(5):482-488. **2.** Rosario N, et al. *Curr Opin Allergy Clin Immunol*. 2011;11(5):471-476. **3.** Winfield AJ, et al. *Br J Ophthalmol*. 1990;74(8):477-480. **4.** Rosin LM, et al. *Clin Ophthalmol*. 2013;7:2131-2135. **5.** Bielory BP, et al. *Acta Ophthalmologica*. 2012;90(5):399-407. **6.** Bielory L, et al. *Allergy Asthma Proc*. 2013;34(5):408-420. **7.** DEXTENZA [prescribing information]. Bedford, MA: Ocular Therapeutix, Inc.; 2019. **8.** Sawhney AS, Jarrett P, Bassett M, Blizzard C, inventors; Incept, LLC, assignee. US patent 8,409,606 B2. April 2, 2020.

# Pooled Analysis of Four DEXTENZA Clinical Studies

## Randomized, Double-masked, Vehicle-controlled Studies in Allergic Conjunctivitis Patients

- **One Phase 2** (PII) and **three Phase 3** (PIII1, PIII2, PIII3) studies
- Used a modified Ora-CAC® (Conjunctival Allergen Challenge) model

**Key Inclusion Criteria**

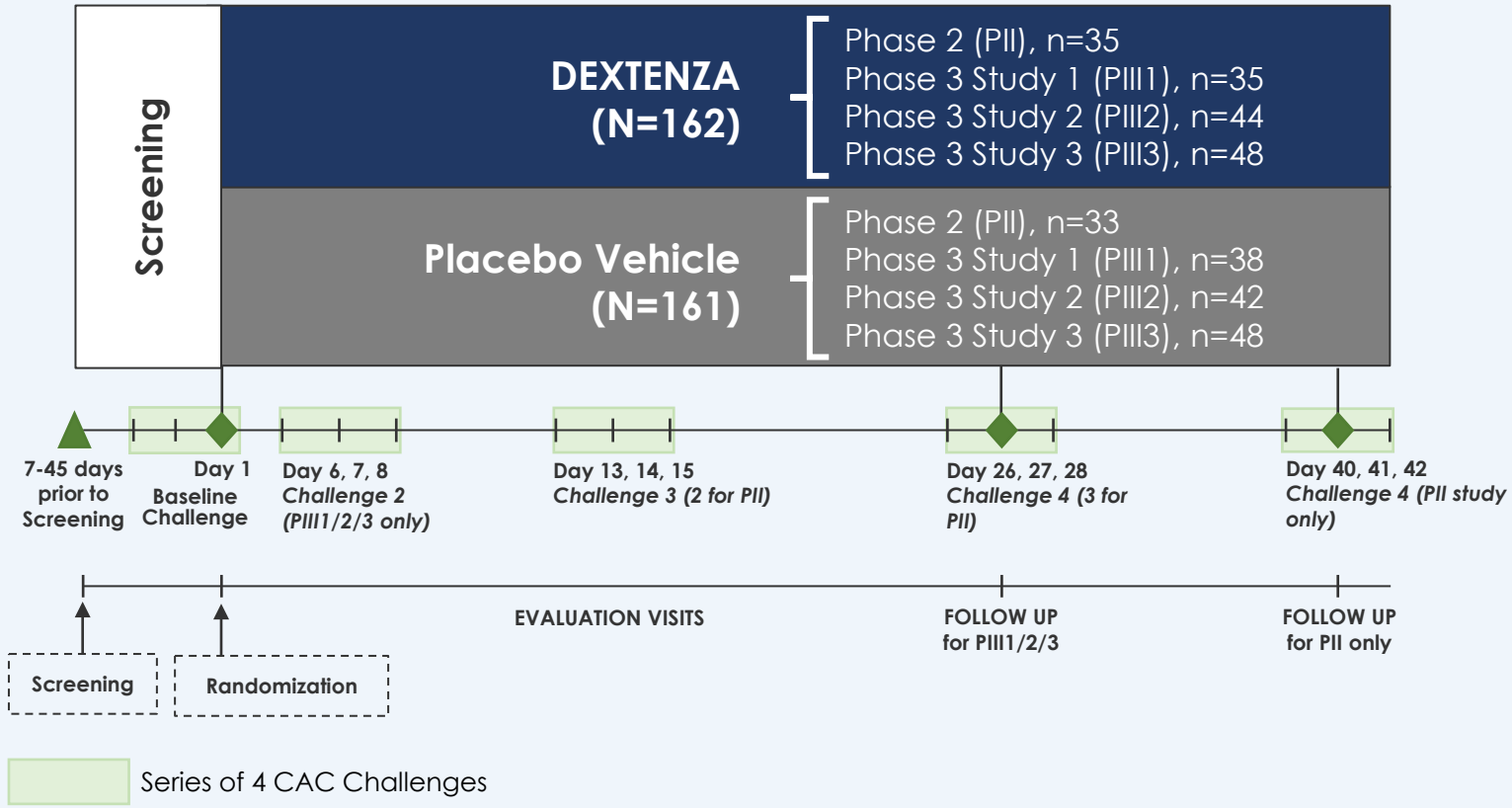
- History of allergic conjunctivitis
- Positive skin test to seasonal and/or perennial allergens
- Bilateral CAC reaction

**Objective**

- To evaluate the safety and efficacy of DEXTENZA for the treatment of signs and symptoms of allergic conjunctivitis

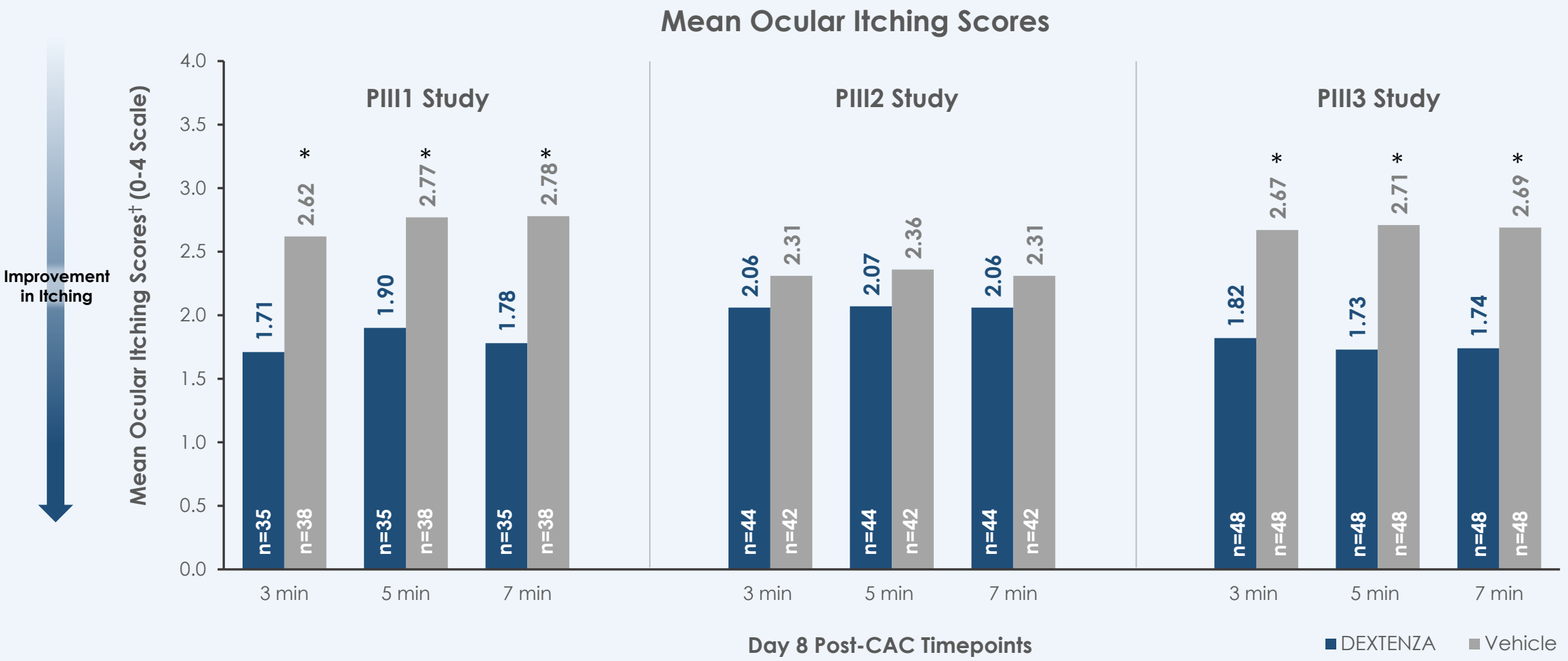
**Endpoints**

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



# Ocular Itching Primary Endpoint by Phase 3 Study

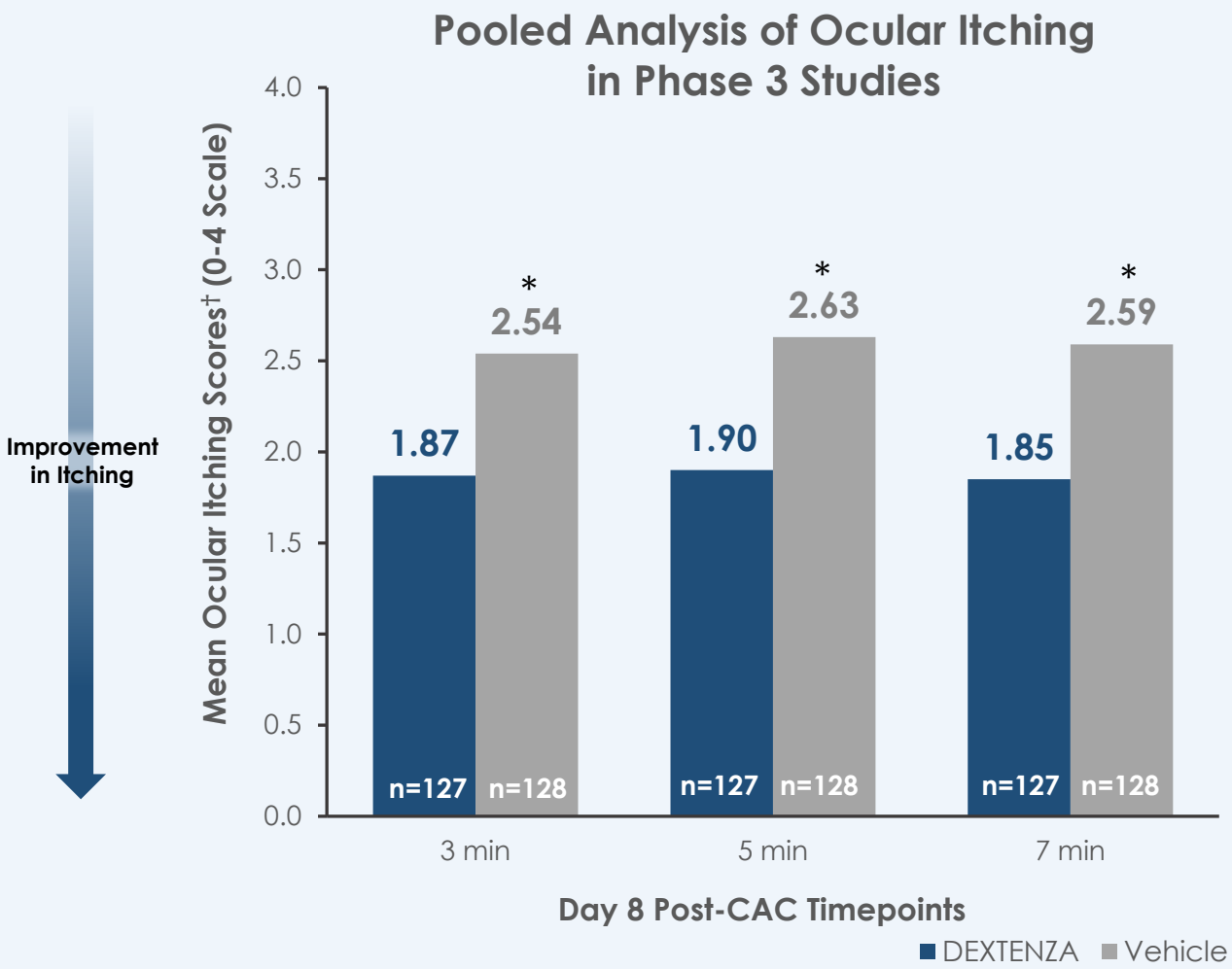
## Subjects treated with DEXTENZA reported significantly lower mean ocular itch scores in two Phase 3 studies

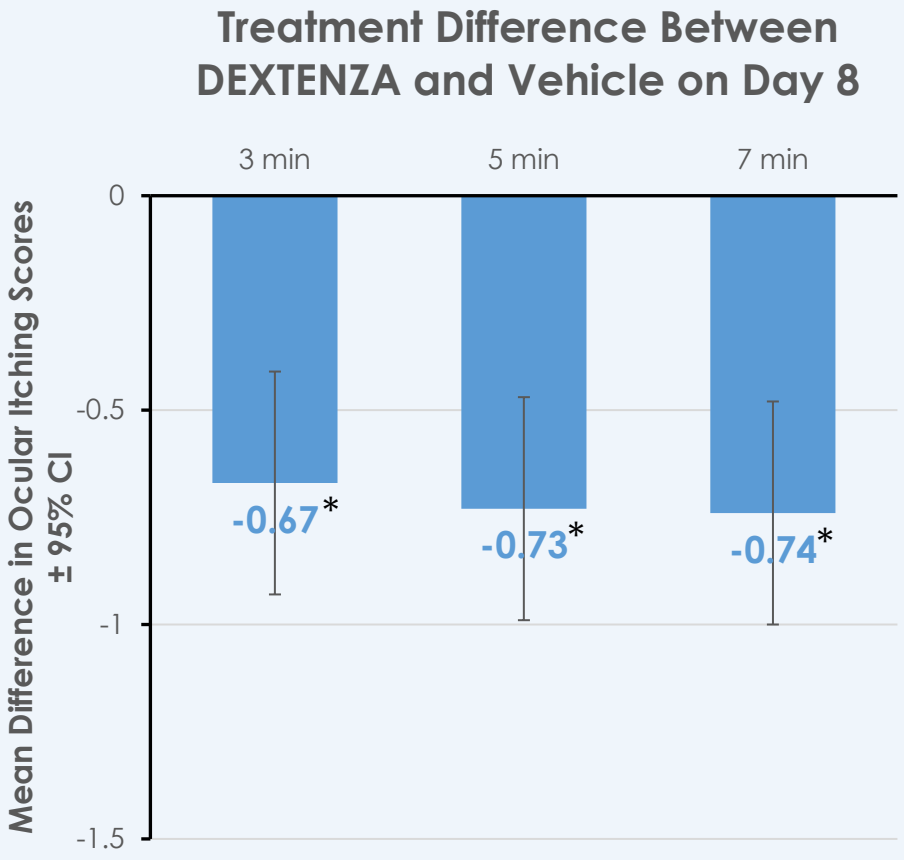



*Statistically significant difference; P<0.0025
† Least square means
Analysis populations: ITT with MCMC
CAC, conjunctival allergen challenge; ITT, intent to treat

# Pooled Analysis of Ocular Itching Primary Endpoint

**DEXTENZA achieved statistically significant lower mean ocular itching scores at all 3 post-CAC timepoints on Day 8**

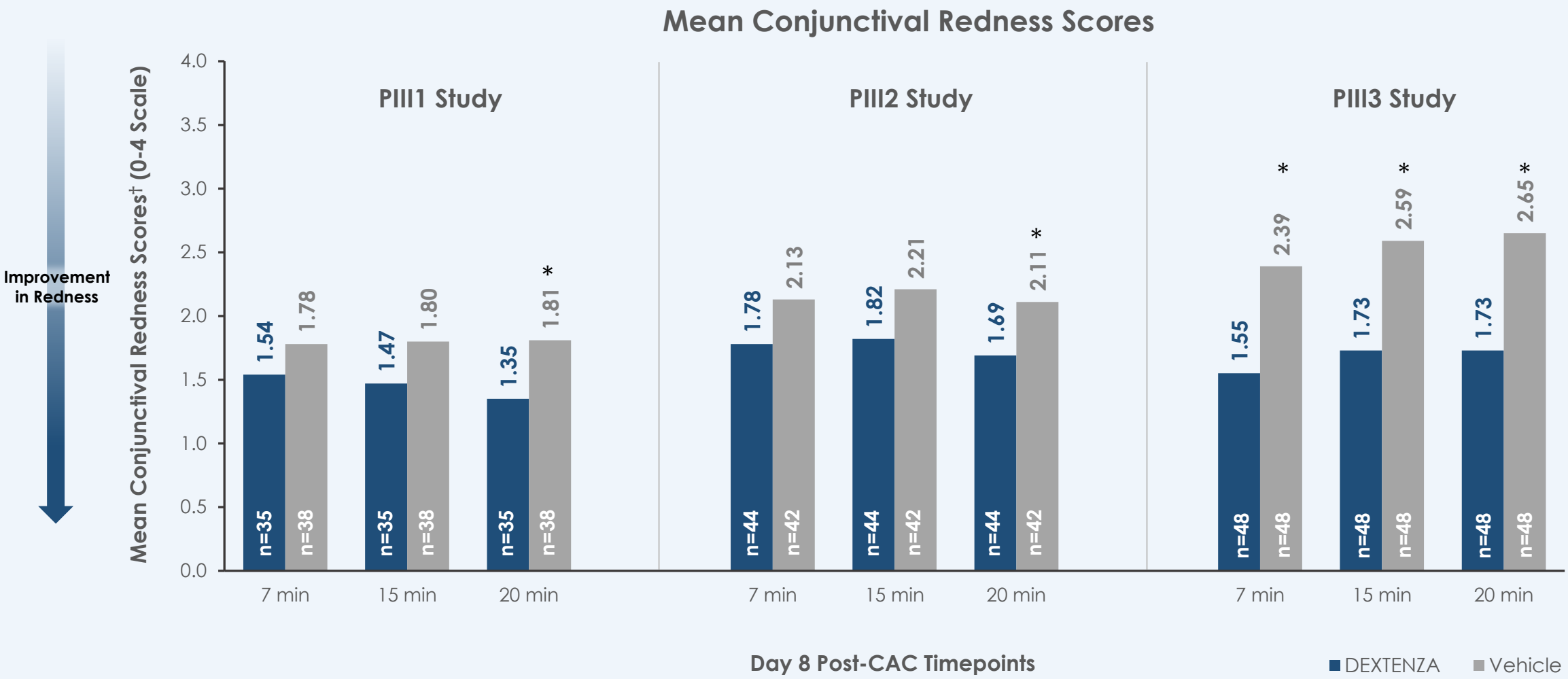



* Statistically significant difference; P<0.0001
† Least square means
Analysis population: ITT with MCMC
CAC, conjunctival allergen challenge; ITT, intent to treat

# Conjunctival Redness Endpoint by Phase 3 Study

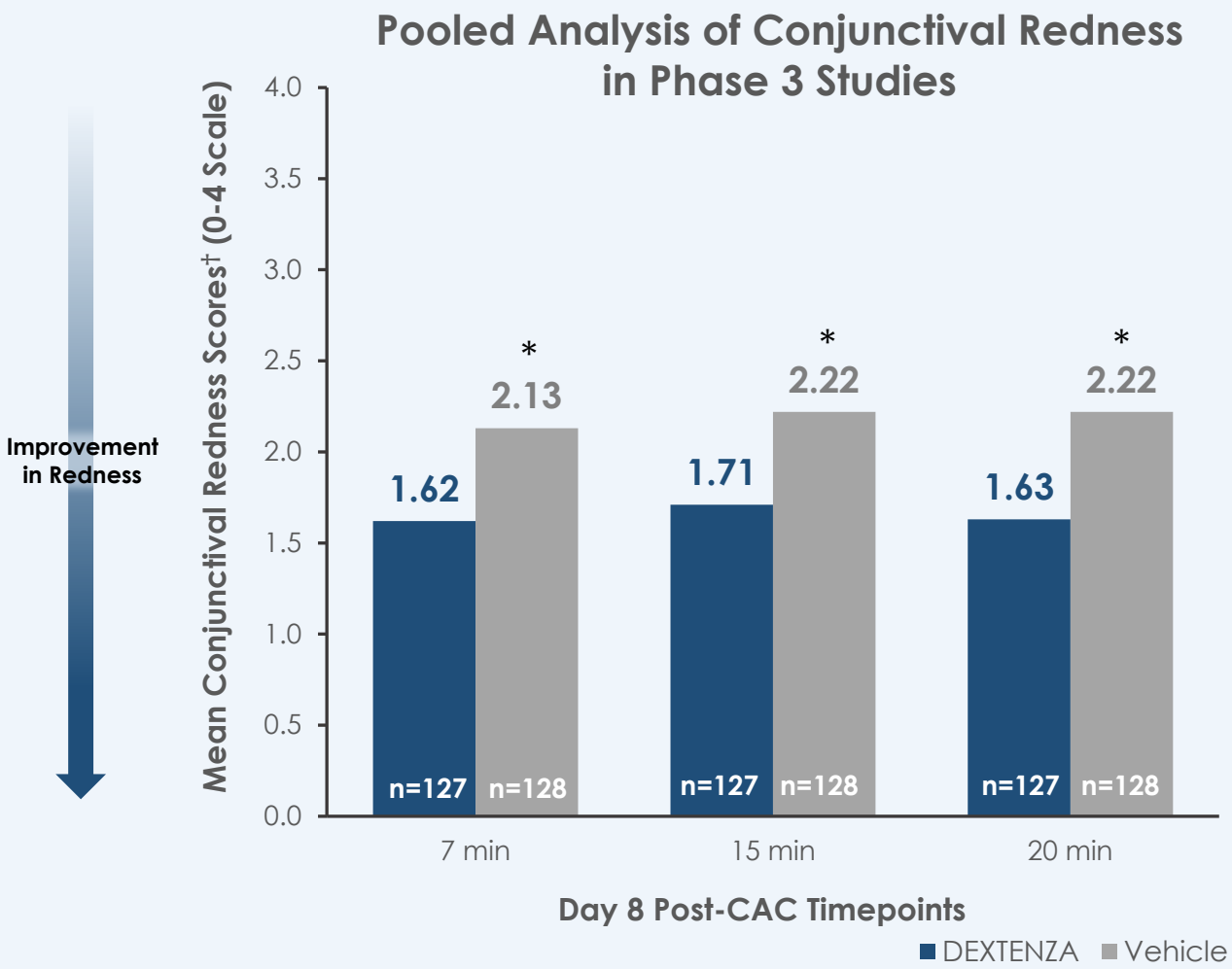
## Study 3 demonstrated significant differences in conjunctival redness scores in favor of DEXTENZA on Day 8

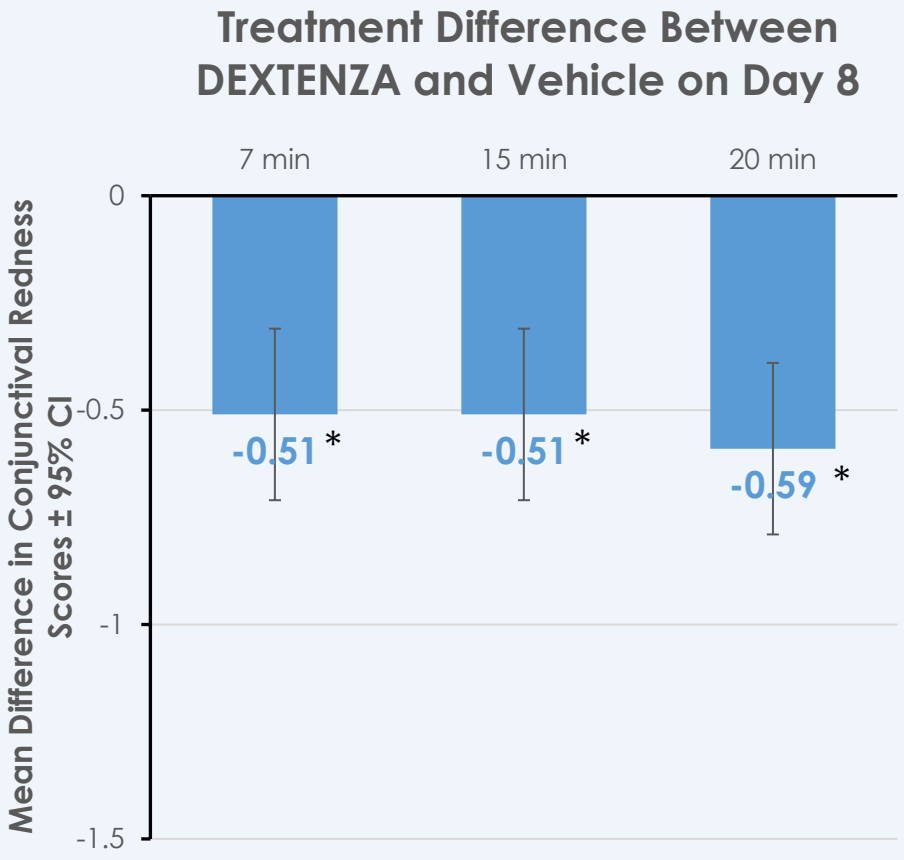



* Statistically significant difference; P<0.05
† Least square means
Analysis populations: ITT with observed data
CAC, conjunctival allergen challenge; ITT, intent to treat

# Pooled Analysis of Conjunctival Redness Endpoint

## DEXTENZA significantly lowered mean conjunctival redness scores at all 3 post-CAC timepoints on Day 8




* Statistically significant difference; P<0.0001
† Least square means
Analysis populations: ITT with observed data only
CAC, conjunctival allergen challenge; ITT, intent to treat

# Summary of Adverse Events

## Lower proportion of DEXTENZA-treated subjects reported AEs compared to the vehicle group

- 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 (hospitalization due to depression) was reported in the DEXTENZA group and was deemed unrelated to treatment by the investigator
- AEs in ≥1% of the DEXTENZA group:
  - Increased IOP (3.2%)
  - Reduced visual acuity (1.3%)
  - Increased lacrimation (1.3%)
  - Eye discharge (1.3%)

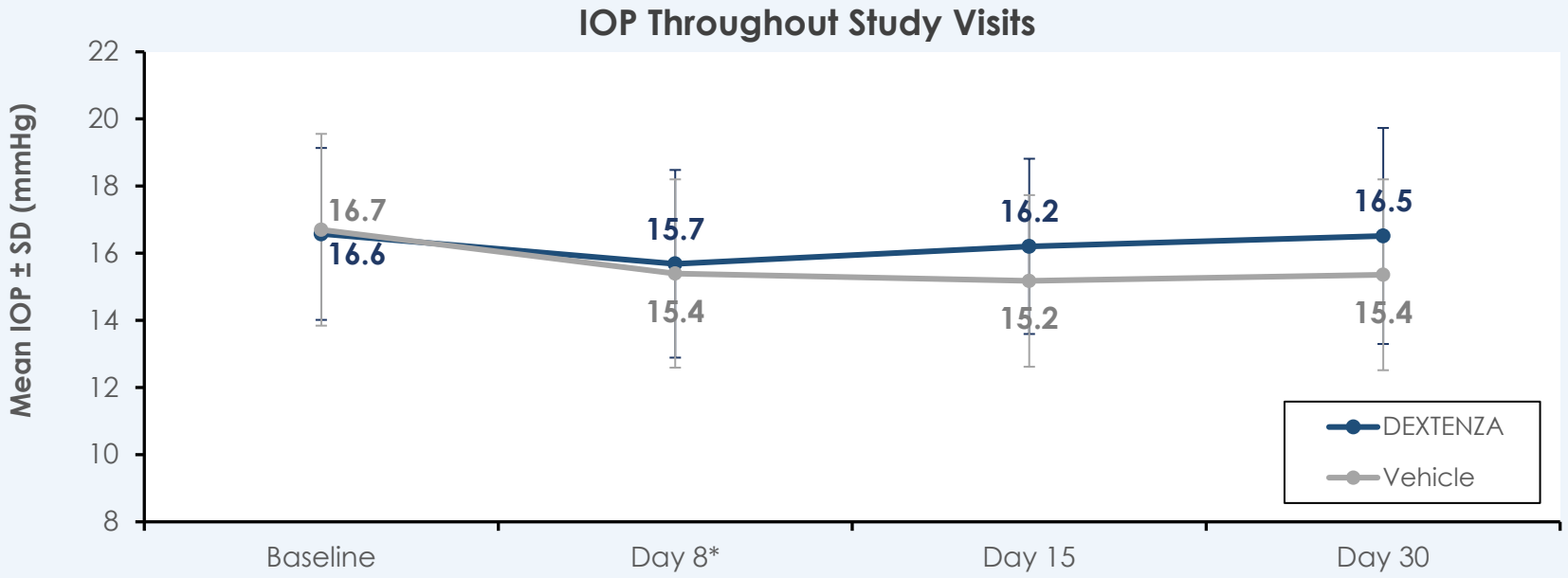
**Safety Summary of Allergic Conjunctivitis Subjects from Four Clinical Trials**

| Subjects with at least one: | DEXTENZA N=154 n (%) | Vehicle N=161 n (%) |
|---|---|---|
| AE | 29 (18.8) | 39 (24.2) |
| Mild | 22 (14.3) | 27 (16.8) |
| Moderate | 7 (4.5) | 12 (7.5) |
| Severe | 0 | 0 |
| Treatment-related AE | 13 (8.4) | 17 (10.6) |
| Ocular AE | 19 (12.3) | 23 (14.3) |
| Treatment-related Ocular AE | 13 (8.4) | 16 (9.9) |
| Serious AE (SAE) | 1 (0.6)* | 0 |
| Treatment-related SAE | 0 | 0 |
| Ocular SAE | 0 | 0 |
| AE Leading to Study Withdrawal | 2 (1.3)† | 1 (0.6) |

* non-ocular SAE (hospitalization due to depression) was not considered related to study treatment and was recovering/resolving upon study completion
† one subject in the PII Study withdrew due to an AE (IOP increased) which resolved. One subject in the PIII3 Study withdrew due to an AE (eye irritation) which resolved.
AE, adverse event

# Intraocular Pressure Events

- IOP elevations (≥10 mmHg increase from baseline or ≥30 mmHg) occurred in 5 subjects (3.2%)
  - None led to removal of DEXTENZA
- Mean IOP was consistently within normal ranges across all study visits




| 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 |

* 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 Clinical Development in Allergic Conjunctivitis

- 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