Safety and Efficacy of OTX-DED, an Intracanalicular Dexamethasone Insert, for the Treatment of Episodic Dry Eye Disease: A Phase 2 Study

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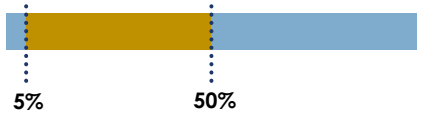
Disclosures

- **Presenter:** Lisa Nijm was an investigator in the current study
- **Co-authors:** William C. Christie and David L. Wirta were investigators in the current study. Betsy Gillick, Rabia Gurses-Ozden, and Michael H. Goldstein are employees of Ocular Therapeutix.
- **Funding:** This clinical trial was funded by Ocular Therapeutix.

This presentation discusses an investigational product, OTX-DED. Its efficacy and safety profile have not been established and it has not been approved by the FDA.

Unmet Needs in Dry Eye Disease Therapy

- Dry eye disease (DED) is a multifactorial disorder of the tears and ocular surface and represents the most common reason for seeking medical eye care[1,2]



Prevalence is ***5***% to **50**% of global population[2]

8.6 million episodic DED patients are treated with prescription or over-the-counter therapies in the US[3]

Prevalence increases with **age** and is 2-3 times higher in the **female** population compared to the male population[4]

- Inflammation plays a key role in DED and corticosteroids are well-established as a fast-acting and effective treatment,[1,5] however:
  - Overuse and/or long-term use of topical ophthalmic steroids can lead to IOP elevations and cataract formation[6]
  - Topical ophthalmic drops may contain preservatives that can lead to corneal toxicity and further aggravate DED[7-9]

A preservative-free corticosteroid for the short-term treatment of DED signs and symptoms that eliminates the potential for drop overuse/misuse by patients is needed

References: 1. Craig JP, et al. *Ocul Surf*. 2017 Jul;15(3):276-283. **2.** Stapleton F, et al. *Ocul Surf*. 2017;15(3):334-365. **3.** 2019 Dry Eye Products Market Report, Market Scope **4.** Dana R, et al. *Am J Ophthalmol*. 2019;202:47-54. **5.** Pflugfelder SC. *Am J Ophthalmol*. 2004;137:337–342. **6.** Yang CQ, et al. *J Zhejiang Univ Sci B*. 2006;7(8):675-678. **7.** EYSUVIS [prescribing information]. Watertown, MA; Kala Pharmaceuticals, Inc; 2020. **8.** Fraunfelder FT, et al. *J Ophthalmol*. 2012;2012:285851. **9.** Epstein SP, et al. *J Ocul Pharmacol Ther*. 2009;25(2):113-119.

OTX-DED (dexamethasone intracanalicular insert)

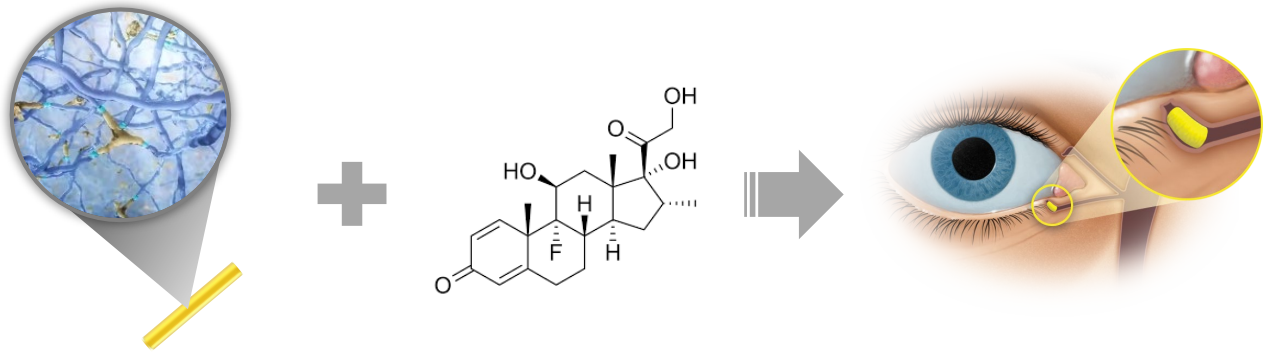
OTX-DED is a novel, hydrogel-based, preservative-free, resorbable intracanalicular insert being evaluated for the short-term treatment of signs and symptoms of DED

Combines two common strategies to treat DED:

- Primarily anti-inflammatory therapy with a sustained and tapered delivery of steroid
- Potentially aids tear conservation through punctal occlusion

Product Attributes

- Designed to provide therapy for 2-3 weeks
- Alternative to conventional steroid eye drops
- Preservative-free
- Fully biodegradable
- Conjungated with fluorescein for visualization



Polyethylene Glycol (PEG) Hydrogel
(Inactive Delivery Platform)

Dexamethasone 0.2 or 0.3 mg
(Active Ingredient)

OTX-DED
(dexamethasone intracanalicular insert)

Phase 2 Study Objective and Design

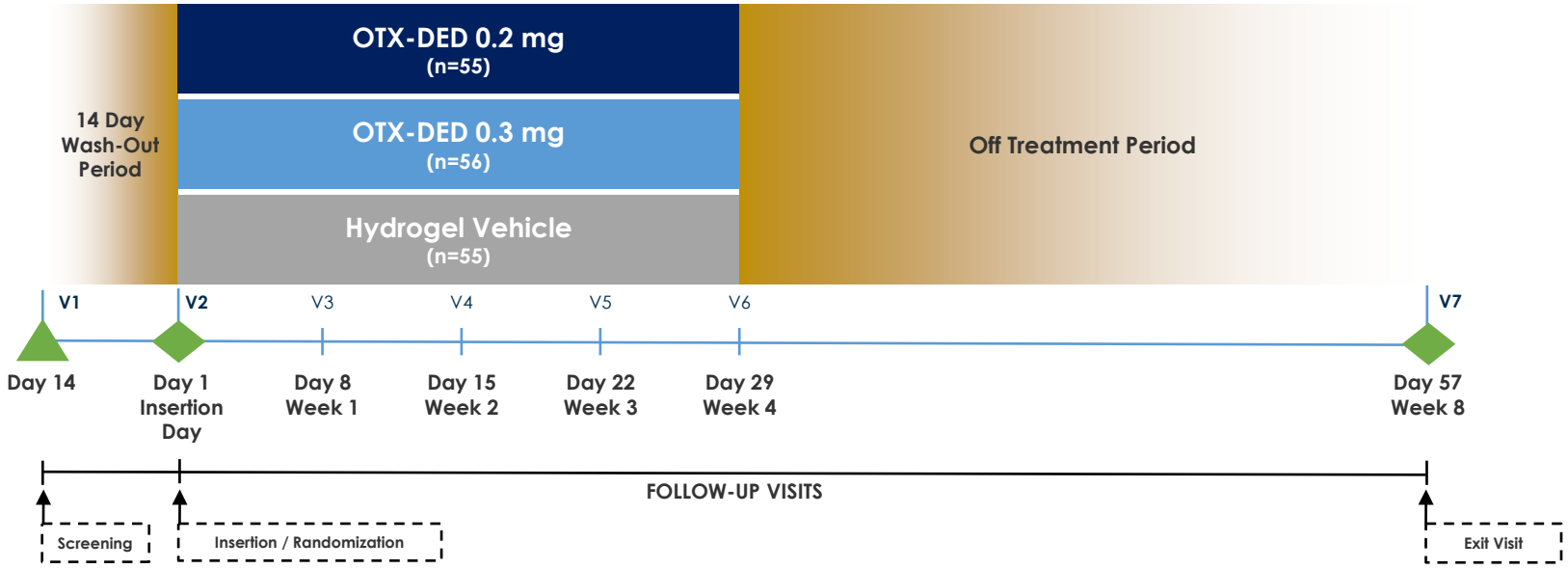
Objective: Safety and efficacy of OTX-DED for the short-term treatment of signs and symptoms of dry eye disease

Design

- Prospective, randomized, double-masked, vehicle-controlled study
- Key inclusion criteria:
  - DED diagnosis in both eyes for ≥6 months
  - Eye dryness severity score (VAS) ≥30
  - Bulbar conjunctival hyperemia grade ≥2 (CCLRU scale)

Endpoints

- Primary endpoint: Bulbar conjunctival hyperemia – worst zone (Day 15)
- Secondary endpoints
  - Bulbar conjunctival hyperemia – individual zones, total
  - Eye Dryness Score (visual analog scale [VAS])
- Safety: Adverse events (ocular and non-ocular)



Abbreviation: CCLRU, Cornea and Contact Lens Research Unit; DED, dry eye disease; VAS, visual analog scale

Outcome Measures

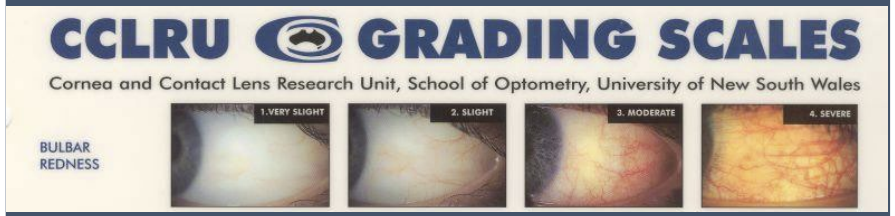
Efficacy Endpoints

- **Signs**
  - **Primary endpoint**: Bulbar conjunctival hyperemia* change from baseline (CFB) at 15 days – worst zone
  - **Secondary endpoint:** Bulbar conjunctival hyperemia* using CCLRU grading scale, CFB, individual zones, and total
- **Symptoms**
  - **Secondary endpoint:** Eye dryness score (visual analog scale [VAS]), CFB, and absolute values at each post-baseline study visit

Safety Endpoints

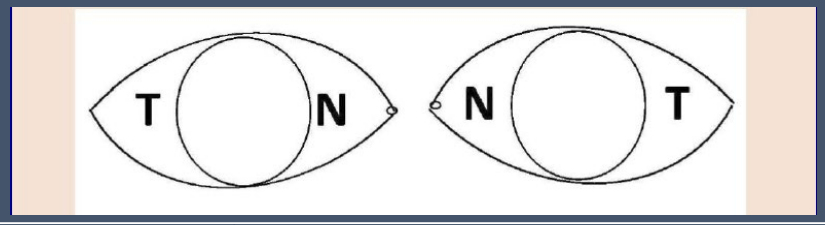
- Adverse events: BCVA, slit-lamp examinations, IOP, dilated fundus exam, artificial tear use during the study

CCLRU Conjunctival Hyperemia Grading Scale



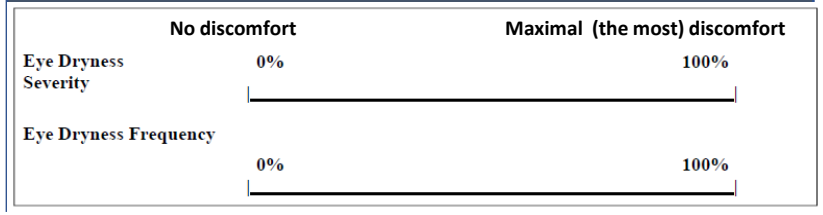
Grade	Scale
0	None
1	Very Slight
2	Slight
3	Moderate
4	Severe

Regions for Conjunctival Hyperemia Grading



Worst Zone	Scale (0-4)
Nasal (N)	Scale (0-4)
Temporal (T)	Scale (0-4)
Frontal	Scale (0-4)
Total	Scale (0-12)

Visual Analogue Scale (VAS) for Eye Dryness



*Bulbar conjunctival hyperemia was assessed photographically at a central reading center using the CCLRU (Cornea and Contact Lens Research Unit) Grading Scale

Demographic and Baseline Measurements

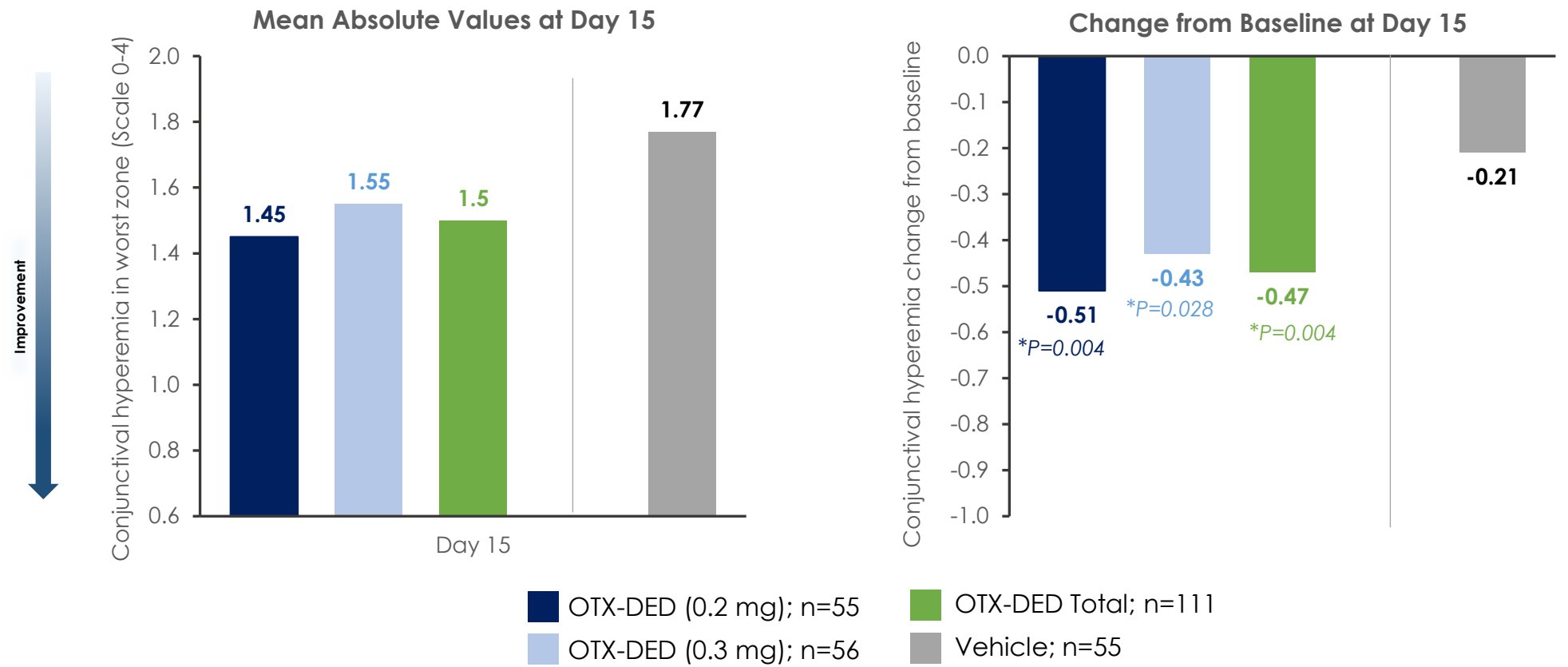
	OTX-DED (0.2 mg)	OTX-DED (0.3 mg)	OTX-DED Total	Vehicle Hydrogel	TOTAL
Modified Intent to Treat (mITT)	**55**	**56**	**111**	**55**	**166**
Age, mean	63.7	65.4	64.6	63.8	64.3
Female, %	74.5	69.6	72.1	74.5	72.9
Race, %					
Caucasian	70.9	67.9	69.4	74.5	71.1
African American	20.0	25.0	22.5	14.5	19.9
Asian	9.1	7.1	8.1	10.9	9.0
BASELINE CHARACTERISTICS (STUDY EYE)					
Mean Conjunctival Hyperemia					
Worst Zone (Scale 0-4)	1.95	1.98	1.96	2.02	1.98
Nasal (Scale 0-4)	1.80	1.88	1.84	1.93	1.87
Temporal (Scale 0-4)	1.67	1.84	1.76	1.89	1.8
Frontal (Scale 0-4)	1.58	1.79	1.68	1.76	1.71
Total (Scale 0-12)	5.05	5.50	5.28	5.58	5.38
Mean Eye Dryness Severity Score (0-100 scale)	72.8	70.0	71.4	72.4	71.7
Mean Eye Dryness Frequency Score (0-100 scale)	73.3	74.5	73.9	74.5	74.1

Number of screen failures: 52 of 224 subjects screened

Primary Efficacy Endpoint

Conjunctival Hyperemia, Worst Zone at Day 15

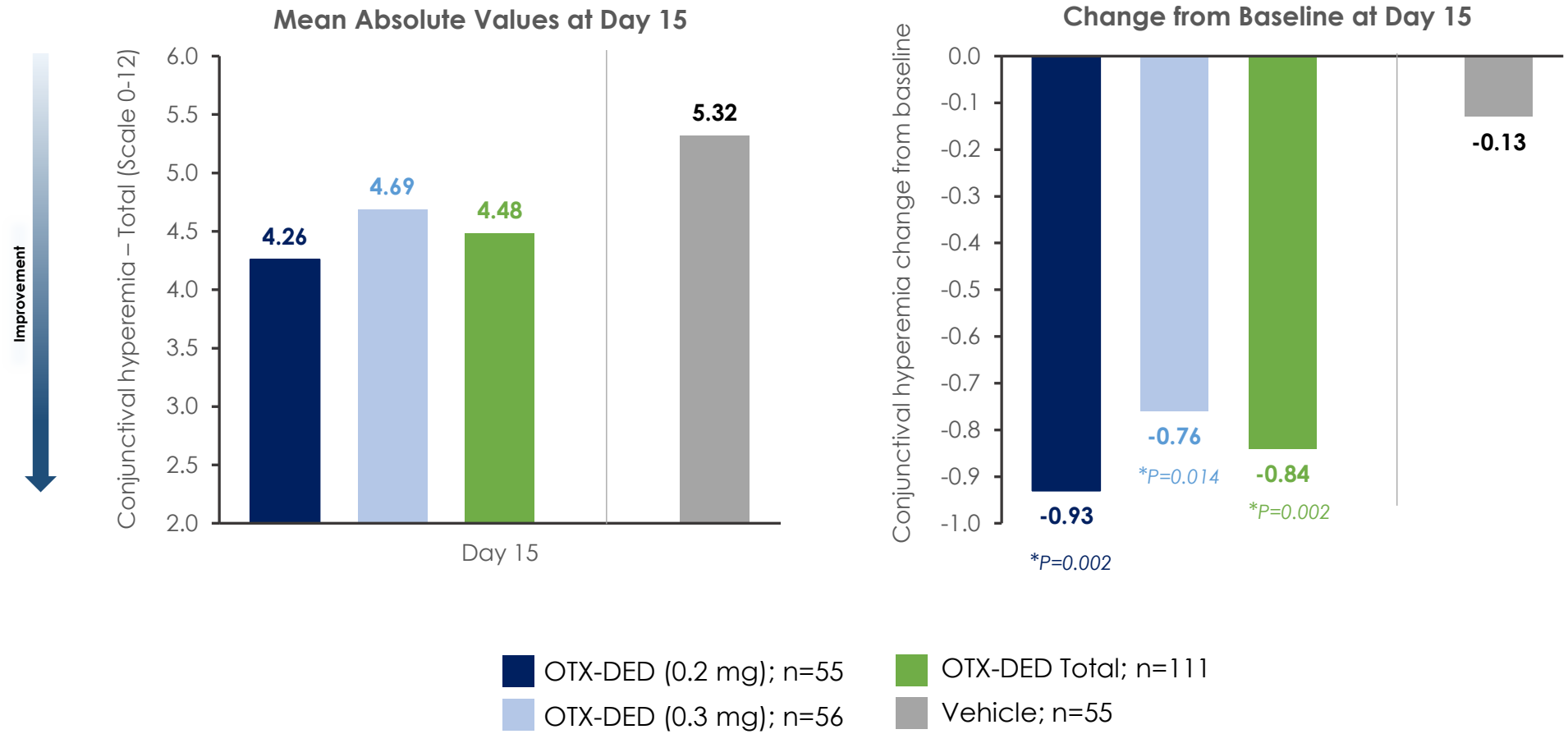
Statistically significant improvement in primary endpoint (conjunctival hyperemia in the worst zone) for OTX-DED relative to vehicle hydrogel for 0.2 and 0.3 mg groups



Sensitivity analysis (MCMC, LOCF, FCS) shows similar results as expected due to minimal data missing (only about 3%)
Modified Intent to Treat Population with Observed Data (N=166); Least Squares Means (LS Means) for change from baseline
*Statistically significant compared to vehicle - P<0.05, Trial not powered to show statistical significance;
MCMC: Markov chain Monte Carlo method; LOCF: Last observation carried forward; FCS: Fully Conditional Specification method

Secondary Efficacy Endpoint

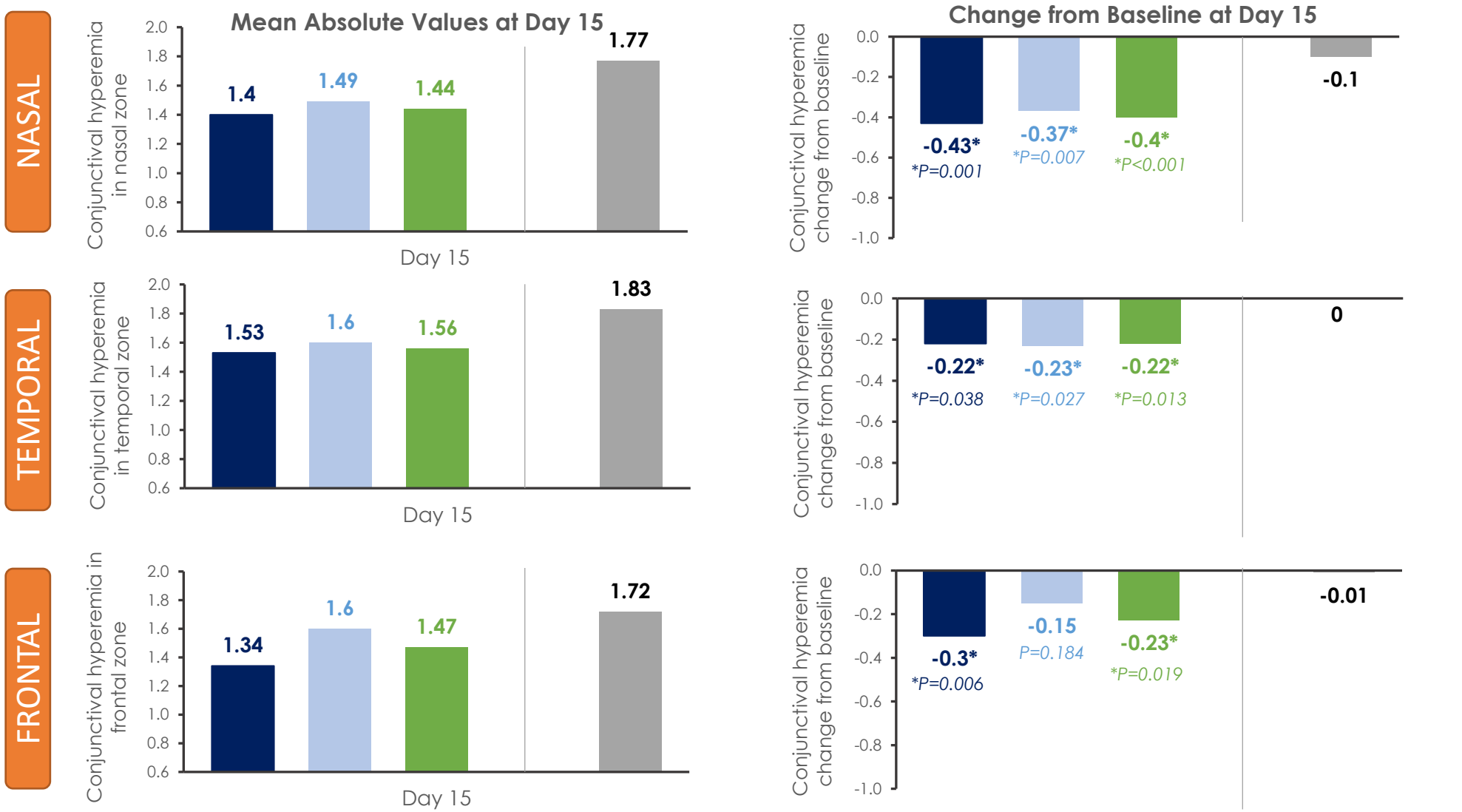
Conjunctival Hyperemia, Total at Day 15



Modified Intent to Treat Population with Observed Data (N=166); Least Squares Means (LS Means) for change from baseline
*Statistically significant compared to vehicle - P<0.05, Trial not powered to show statistical significance

Secondary Efficacy Endpoint

Conjunctival Hyperemia Nasal, Temporal & Frontal at Day 15

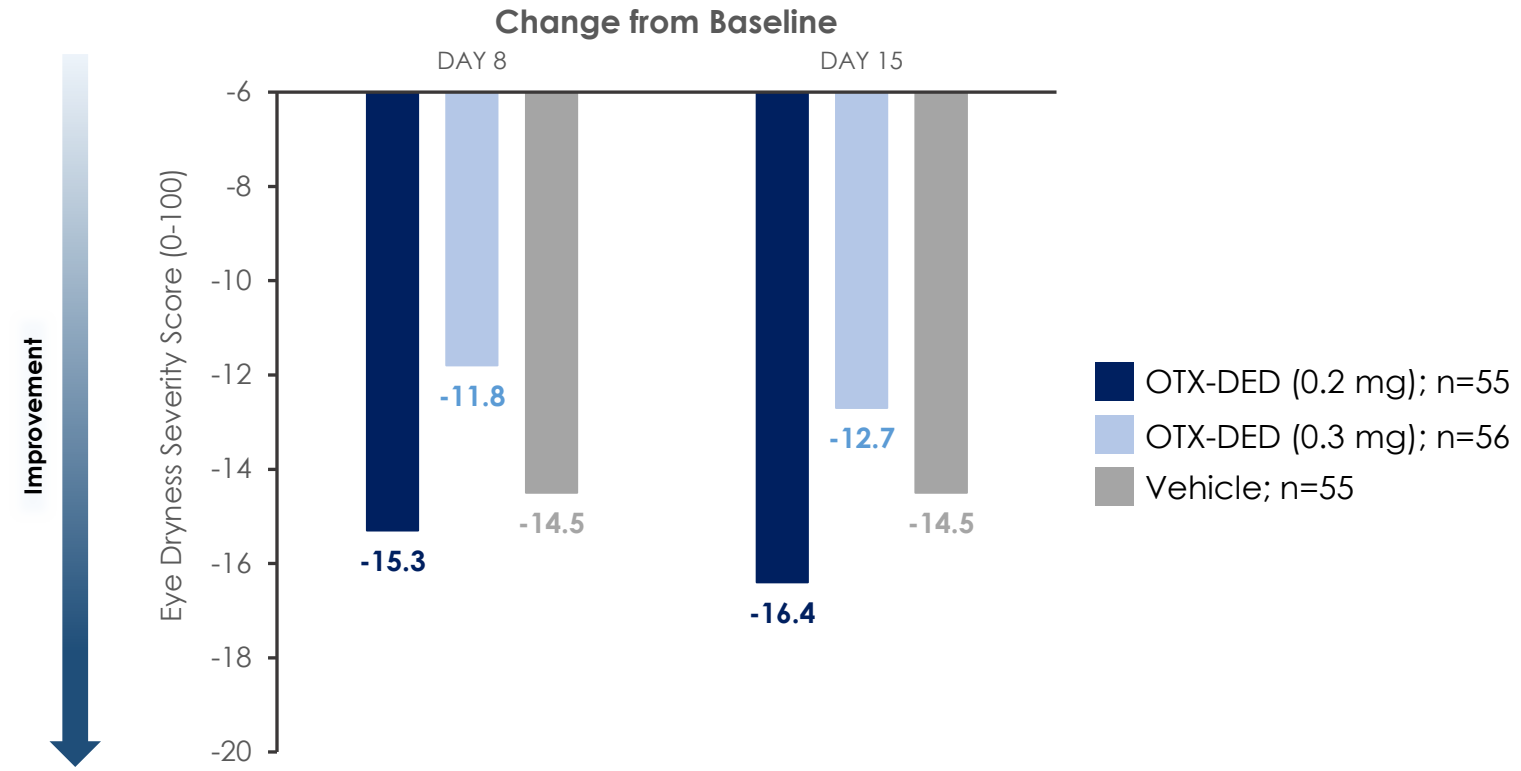


Modified Intent to Treat Population with Observed Data (N=166); Least Squares Means (LS Means) for change from baseline
*Statistically significant compared to vehicle - P<0.05, Trial not powered to show statistical significance;
Nasal, Temporal and Frontal: Scale 0-4

Secondary Efficacy Endpoint

Symptom: Eye Dryness Score (VAS) Severity

Eye dryness severity scores improved from baseline in 0.2 mg & 0.3 mg groups with little separation between active groups and vehicle



BASELINE SCORES	OTX-DED (0.2 mg) n=55	OTX-DED (0.3 mg) n=56	Vehicle Hydrogel n=55
Mean Eye Dryness Severity Score (0-100 scale)	72.8	70.0	72.4

Modified Intent to Treat Population with Observed Data (N=166); Least Squares Means (LS Means) for change from baseline

Treatment-Emergent Adverse Events

- Most common adverse events in OTX-DED treated groups were epiphora/increased lacrimation (8.1%) and IOP elevation (3.6%)
- No ocular serious adverse events or dacryocanaliculitis events were reported

	OTX-DED (0.2 mg) n=55	OTX-DED (0.3 mg) n=56	OTX-DED Total n=111	Vehicle Hydrogel n=55	All Subjects N=166
Subjects with at least 1 TEAE, n (%)	12 (21.8%)	13 (23.2%)	25 (22.5%)	11 (20.0%)	36 (21.7%)
Subjects with at least 1 Ocular TEAE, n (%)	7 (12.7%)	12 (21.4%)	19 (17.1%)	7 (12.7%)	26 (15.7%)
Subjects with at least 1 non-ocular TEAE, n (%)	5 (9.1%)	2 (3.6%)	7 (6.3%)	4 (7.3%)	11 (6.6%)
Serious Adverse Events (SAEs), n	0	0	0	2	2†
Ocular SAEs, n	0	0	0	0	0
Most Common Ocular AEs					
Eye Pruritus, n (%)	1 (1.8%)	0	1 (0.9%)	2 (3.6%)	3 (1.8%)
Lacrimation Increase, n (%)	2 (3.6%)	7 (12.5%)	9 (8.1%)	2 (3.6%)	11 (6.6%)
IOP Elevation, n (%)	2 (3.6%)	2 (3.6%)	4 (3.6%)	0	4 (2.4%)
Most Common Non-ocular AEs					
COVID-19, n (%)	1 (1.8%)	0	1 (0.9%)	0	1 (0.6%)
Arthralgia, n (%)	1 (1.8%)	1 (1.8%)	2 (1.8%)	0	2 (1.2%)

†Serious Adverse Events were Cellulitis and COVID Pneumonia both in the vehicle group
Severe Adverse Events were Epiphora in 0.2 mg OTX-DED group & Cellulitis and COVID Pneumonia in the vehicle group

Modified Intent to Treat Population with Observed Data (N=166)

Conclusions

Phase 2 Study Evaluating Safety and Efficacy of OTX-DED in Dry Eye Subjects

- Statistically significant improvement in the primary endpoint (bulbar conjunctival hyperemia in the worst zone on Day 15) for OTX-DED relative to vehicle hydrogel for 0.2 and 0.3 mg groups
  - Trial was not powered for statistical significance
  - Sensitivity analysis showed similar results
- Conjunctival hyperemia grade in the total, nasal, temporal, and frontal zones improved with OTX-DED relative to vehicle hydrogel on Day 15
  - All statistically significant except for frontal zone OTX-DED 0.3 mg group
- Eye dryness score (symptom endpoint) improved from baseline in all three groups, with no separation between active groups and vehicle
  - Post-hoc analysis shows potential opportunities to differentiate between OTX-DED and vehicle hydrogel groups
- Most common adverse events in OTX-DED treated groups (0.2 & 0.3 mg) were epiphora/lacrimation increase (8.1%), and IOP elevation (3.6%)
  - No ocular serious adverse events were reported
  - Low rates of ocular pain/discomfort/irritation