Efficacy and Safety of OTX-DED Dexamethasone Intracanalicular Insert in Subjects with Dry Eye Disease: A Multicenter, Randomized, Vehicle-Controlled Phase 2 Study

Lisa Nijm, MD, JD[1]; Joseph Tauber, MD[2]; David G. Evans, OD[3]; Betsy Gillick[4]; Rabia Gurses-Ozden, MD[4]; Michael H. Goldstein, MD[4]

[1]Warenville Eye Care and LASIK Center, Warrenville, IL; [2]Tauber Eye Center, Kansas City, MO; [3]Total Eye Care, Memphis, TN; [4]Ocular Therapeutix, Inc., Bedford, MA

BACKGROUND

- Many patients with dry eye disease (DED) suffer from episodic flare-ups that require an effective short-term treatment[1-4]
- Approved therapies for the chronic treatment of DED are known for slow onset of action and burning/stinging upon instillation[5-8]
- All currently approved topical steroid eye drops in the US have preservatives that may exacerbate ocular surface diseases[5-10]
- OTX-DED is a physician-administered, biodegradable, preservative-free, hydrogel-based insert that is placed into the canaliculus and releases dexamethasone to the ocular surface for 2-3 weeks (presented in **Figure 1**)

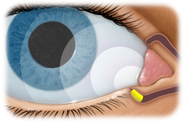


Figure 1. Rendering of OTX-DED inserted into the canaliculus

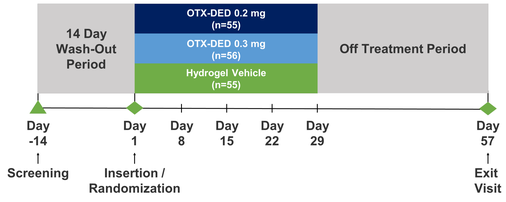
STUDY OBJECTIVE

To evaluate the efficacy and safety of OTX-DED for the short-term treatment of signs and symptoms of dry eye disease

METHODS

- Prospective, randomized, double-masked, vehicle-controlled, Phase 2 clinical trial (NCT04747977; presented in **Figure 1**)

Figure 1. Study Design of OTX-DED Phase 2 Clinical Trial



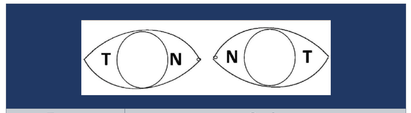
- Key Inclusion Criteria:
  - DED diagnosis in both eyes for ≥6 months
  - Eye dryness severity score (VAS) ≥30
  - Bulbar conjunctival hyperemia grade ≥ 2 (CCLRU scale)

METHODS (Con't)

PRIMARY ENDPOINT

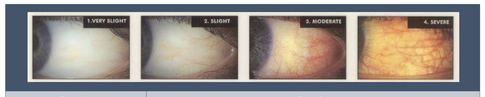
- Change from baseline in bulbar conjunctival hyperemia in the worst zone on Day 15 (presented in **Figure 2**)
  - Assessed photographically by a central reading center using the CCLRU grading scale (presented in **Figure 3**)

Figure 2. Grading Zones for Bulbar Conjunctival Hyperemia



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

Figure 3. CCLRU Bulbar Hyperemia Grading Scale

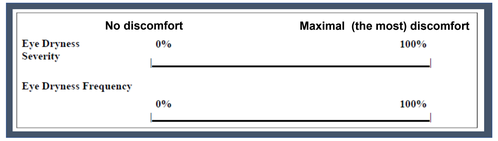


Grade	Scale
0	None
1	Very Slight
2	Slight
3	Moderate
4	Severe

SECONDARY ENDPOINTS

- Change from baseline in bulbar conjunctival hyperemia in individual zones and total
- Change from baseline and absolute values of Eye Dryness Score using a visual analog scale (VAS) presented in **Figure 4**

Figure 4. Visual Analogue Scale for Eye Dryness



RESULTS

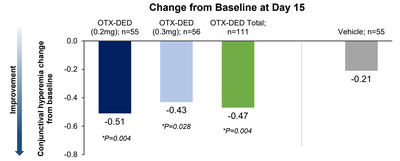
Table 1. Demographics and Baseline Characteristics of Enrolled Subjects

	OTX-DED (0.2 mg)	OTX-DED (0.3 mg)	OTX-DED Total	Vehicle Hydrogel	All Subjects
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 Conjunctival Hyperemia, mean					
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
Baseline Eye Dryness Severity Score, mean (0-100 scale)	72.8	70.0	71.4	72.4	71.7
Baseline Eye Dryness Frequency Score, mean (0-100 scale)	73.3	74.5	73.9	74.5	74.1

BULBAR CONJUNCTIVAL HYPEREMIA

- Subjects that received OTX-DED 0.2 or 0.3 mg demonstrated a statistically significant improvement in conjunctival hyperemia at Day 15 (primary endpoint) compared to subjects that received hydrogel vehicle inserts (presented in **Figure 5**)

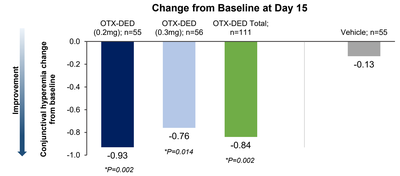
Figure 5. Primary Endpoint: Conjunctival Hyperemia in the Worst Zone at Day 15



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;

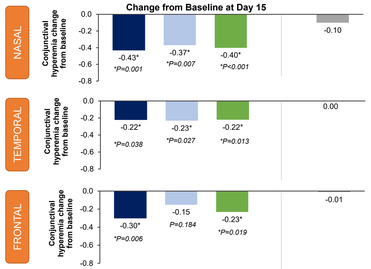
- Improvements in bulbar conjunctival hyperemia scores on Day 15 in individual and total zones in the OTX-DED 0.2 and 0.3 mg groups were all statistically significant when compared to the hydrogel vehicle group except for OTX-DED 0.3 mg frontal zone (**Figure 6 and 7**)

Figure 6. Secondary Endpoint: Total Conjunctival Hyperemia Grade 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

Figure 7. Secondary Endpoint: Conjunctival Hyperemia in Individual Zones at Day 15

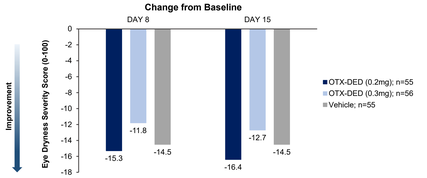


Modified Intent to Treat Population with Observed Data (N=166); Least Squares Means (LS Means) for change from baseline
*Statistically significant compared to vehicle - p<0.05, Trial not powered to show statistical significance;
Nasal, Temporal and Frontal: Scale 0-4

EYE DRYNESS SEVERITY SCORE

- Eye Dryness Severity scores improved from baseline in the OTX-DED 0.2 and 0.3 mg groups with little separation of effect between the active groups and hydrogel vehicle (presented in **Figure 8**)

Figure 8. Change from Baseline in Eye Dryness Severity Score (VAS)

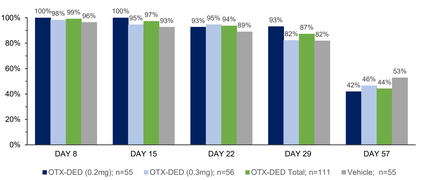


Modified Intent to Treat Population with Observed Data (N=166); Least Squares Means (LS Means) for change from baseline
*Statistically significant compared to vehicle - p<0.05, Trial not powered to show statistical significance;
Nasal, Temporal and Frontal: Scale 0-4

RETENTION OF INSERTS

- Retention assessed by visualization of the insert was high throughout the 30-day study period (presented in **Figure 9**)

Figure 9. Retention Rates



SAFETY OUTCOMES

Table 2. Number of Subjects with Adverse Events

	OTX-DED (0.2 mg) n=55	OTX-DED (0.3 mg) n=56	OTX-DED Total n=111	Vehicle Hydrogel n=55	All Subject 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

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

- The most common ocular adverse events in the OTX-DED treated groups were epiphora (lacrimation increase; 8.1%) and IOP elevation (3.6%) as presented in **Table 3**
- There were no ocular SAEs or dacryocanaliculitis events reported

Table 3. Most Common Ocular and Non-ocular AEs

	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
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%)

CONCLUSIONS

- Subjects treated with OTX-DED 0.2 and 0.3 mg demonstrated a statistically significant improvement in the primary endpoint (bulbar conjunctival hyperemia in the worst zone) compared to hydrogel vehicle
- Symptoms (eye dryness score) improved from baseline in all three groups, with little separation between active groups and vehicle
- No ocular SAEs were reported with OTX-DED and the most common AE was epiphora (8.1%) and elevated IOP (3.6%)
- OTX-DED is a potential candidate for the short-term treatment of signs and symptoms of dry eye disease

Disclosures: LMN, JT, and DGE were investigators in this clinical trial. BG, RGO, and MHG are employees of Ocular Therapeutix, Inc.

Funding: This study was sponsored by Ocular Therapeutix, Inc.

Abbreviations: CCLRU, Cornea and Contact Lens Research Unit; DED, dry eye disease; IOP, intraocular pressure; SAE, serious adverse event; TEAE, treatment-emergent adverse event; VAS, visual analog scale

References: **1**. Bron AJ, et al. *Ocul Surf.* 2017;15:438-510. **2.** Amparo F, et al. *Ocul Surf.* 2018;16(2):249-253. **3.** Iyer JV, et al. *The Scientific World Journal.* 2012;589875. **4.** Kim Y, et al. *Cornea.* 2019;38(12):1483-1488. **5.** RESTASIS [prescribing information]. Irvine, CA; Allergan, Inc; 2012. **6.** CEQUA [prescribing information]. Cranbery, NJ; Sun Pharmaceuticals; 2018. **7.** XIIDRA [prescribing information]. Lexington, MA; Shire US Inc.; 2016. **8.** EYSUVIS [prescribing information]. Watertown, MA; Kala Pharmaceuticals, Inc; 2020. **9.** Fraunfelder FT, et al. *J Ophthalmol.* 2012;2012:285851. **10.** Epstein SP, et al. *J Ocul Pharmacol Ther.* 2009;25(2):113-11

Presented at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting in Denver, CO | May 2, 2022