Safety and Pharmacodynamic Assessment of Repeated Intracameral Travoprost Implant Administration in Beagle Dogs

Charles D. Blizzard; Chintan Patel, PhD; Jeremy Hartman; Sean Serell; Kevin Yeh; Andrew Vanslette; Peter K. Jarrett, PhD; Rabia Gurses-Ozden, MD; Michael H. Goldstein, MD

BACKGROUND

- Lowering intraocular pressure (IOP) is critical to slowing glaucoma progression and is commonly achieved with topical therapy.[1,2]
- However, poor adherence to topical drops has been well documented in glaucoma patients which can impact IOP control management[3-5]
- OTX-TIC is an intracameral implant containing travoprost particles formulated into a hydrogel matrix **(Figure 1):**
  - Delivers therapeutic levels of travoprost for 4-6 months
  - Preservative-free
  - Fully biodegradable
  - Alternative to traditional chronic drop therapy
- Monitoring corneal thickness and endothelial cell density is important in evaluating intracameral inserts as changes may suggest damage to the corneal endothelium
- Preclinical studies in beagles have demonstrated an acceptable safety profile, maintenance of drug levels in the aqueous humor, and a sustained lowering of IOP following injection of a single OTX-TIC implant.[6,9] The current study evaluates the safety and pharmacodynamic profile of repeated dosing and multiple implants of OTX-TIC in beagle dogs.

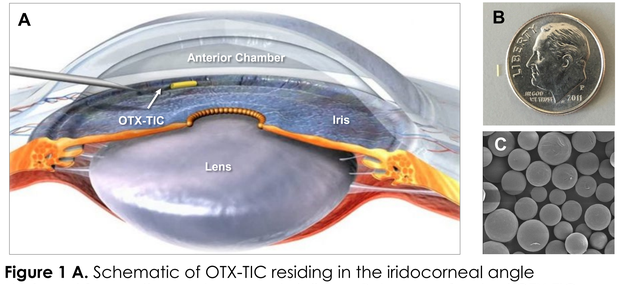


Figure 1 A. Schematic of OTX-TIC residing in the iridocorneal angle designed for continuous travoprost delivery. **B.** Image of actual OTX-TIC implant **C.** SEM image of travoprost-loaded microparticles in fully biodegradable hydrogel vehicle

STUDY OBJECTIVE

To evaluate the safety, tolerability, and pharmacodynamic profile of repeated OTX-TIC administrations and multiple implants in canines

METHODS

Study Design

- OTX-TIC implant(s) containing different doses of travoprost were injected into the anterior chamber of the left eye in normotensive beagle dogs (**Table 1**)
  - Group 2 represents an intended clinical dose
  - Group 3 provides a 2X dose multiple and 2X implant safety factor for travoprost drug and implant biomaterial
  - Group 4 used a shorter persisting hydrogel with a daily travoprost dose comparable to Group 2.

Table 1. Treatment Groups

Group	OS	OD	Dosing Frequency	Number of Animals
1	Two Placebo implants	One Placebo implant	Q18W (Days 1 & 127)	8
2	Sham injection	One OTX-TIC 26 µg implants	Q18W (Days 1 & 127)	8
3	None	Two OTX-TIC 26 µg implants	Q18W (Days 1 & 127)	8
4	Sham injection	One OTX-TIC 13 µg implants	Q8W (Days 1, 57, 113, & 169)	8

Safety Assessments

- Ophthalmic exams and gonioscopic exams were performed
- Corneal thickness was measured using an ultrasound pachymeter
- Endothelial cell count was measured using noncontact specular microscopy

Pharmacodynamic Assessments

- IOP measurements were collected using a rebound tonometer
- Conjunctival hyperemia and miosis are known pharmacodynamic responses to travoprost in dogs and was graded using a modified Hackett-McDonald Scoring System (**Table 2**)

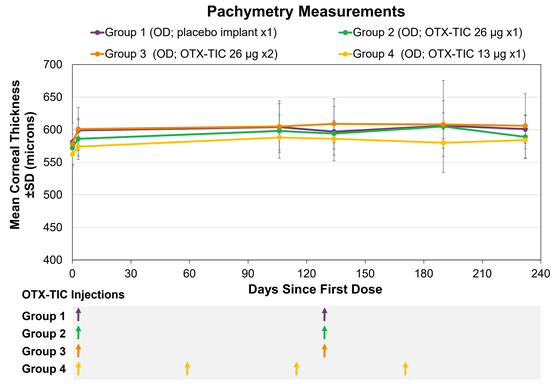
Table 2. Modified Hackett-McDonald Scoring System used to grade pupillary light reflex and conjunctival hyperemia

Score	Pupillary Light Reflex	Conjunctival Hyperemia
0	Normal	Normal
1	Pupil is relatively dilated with sluggish pupillary reflex	Flushed reddish color
2	Pupil is fully dilated with no pupillary reflex	Bright red color
3	Miotic pupil	Dark, beefy red color

RESULTS

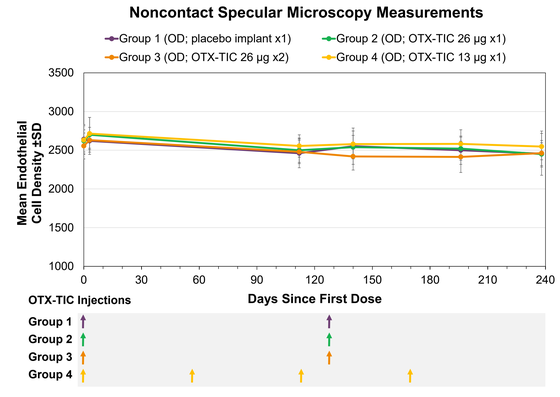
Corneal Thickness

- No statistically significant changes or clinically meaningful abnormalities in corneal thickness were observed following multiple injections of one or two OTX-TIC implants over the course of the study



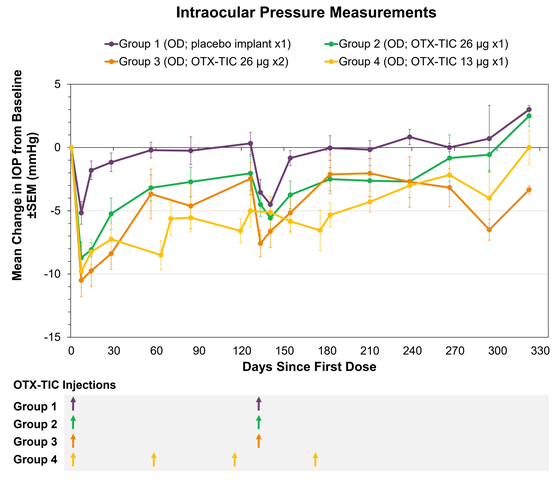
Endothelial Cell Density

- No clinically meaningful or statistically significant changes in ECD were observed following multiple injections of one or two OTX-TIC implants over the course of the study



Intraocular Pressure

- Eyes treated with OTX-TIC implants (OD Groups 2, 3, & 4) had lower IOP compared to eyes treated with one placebo implant (OD Group 1)
- Mean IOP reductions suggest one 26 µg implant (Group 2) had comparable efficacy to two 26 µg implants (Group 3)
- Comparable frequency of statistically significant IOP reductions was noted between one 26 µg implant Q18W (Group 2) and one 13 µg implant Q8W (Group 4)



Conjunctival Hyperemia & Pupillary Reflex

- As expected for PGAs in dogs, mean conjunctival hyperemia and pupillary reflex scores were greater in OTX-TIC treated eyes (Groups 2, 3 and 4 OD) compared to placebo implant (Group 1)
  - For OTX-TIC eyes, mild to moderate hyperemia (+1 to +2) and miosis (+3) were commonly observed throughout the study period
  - Most placebo implant eyes exhibited no miosis (0) and only mild (+1), transient hyperemia for 2 to 7 days post-dose which was considered injection procedure-related

CONCLUSIONS

- **In a canine model, multiple injections of one or two OTX-TIC intracameral implant(s) did not cause significant or clinically meaningful changes in corneal health**
- **Groups treated with OTX-TIC had significant reductions in IOP compared to placebo implant**
- **OTX-TIC is currently being investigated for the treatment of glaucoma in a Phase 2 clinical trial in the US.**

Disclosures: All authors are employees of Ocular Therapeutix, Inc. | This poster presentation discusses an investigational product, OTX-TIC. Its efficacy and safety profile have not been established and it has not been approved by the FDA. | This study was funded by Ocular Therapeutix, Inc.

Abbreviations: ECD, endothelial cell density; OD, right eye; OS, left eye; PGA, prostaglandin analogues; Q18W, every 18 weeks; Q8W, every 8 weeks; SEM, scanning electron microscope

References: 1. Noecker RJ. *Ther Clin Risk Manag*. 2006;2(2):193-206. **2.** Quigley HA, et al. *Br J Ophthalmol.* 2006;90(3):262-267. **3.** Olthoff CMG, et al. *Ophthalmology*. 2005;112(6):953-961. **4.** Schwartz GF, et al. *Surv Ophthalmol.* 2008;53 Suppl1:S57-68. **5.** Nordstrom BL, et al. *Am J Ophthalmol.* 2005;140(4):598-606. **6.** Blizzard CD, et al. *Invest Ophthalmol Vis Sci.* 2018;59(9):1245. **7.** Driscoll A, et al. *Invest Ophthalmol Vis Sci.* 2018;59(9):1250. **8.** Blizzard CD, et al. *Invest Ophthalmol Vis Sci.* 2019;60(9):3777. **9.** Driscoll A, et al. *Invest Ophthalmol Vis Sci.* 2019;60(9):3345.

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