Preclinical Safety and Tolerability of Repeated Intracameral Travoprost Implant (OTX-TIC) Administrations

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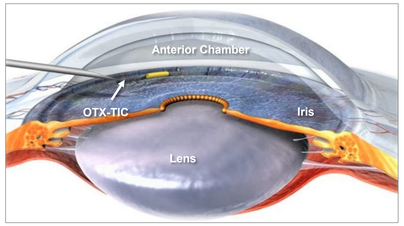
PURPOSE

- 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 a fully bioresorbable, preservative-free, intracameral implant designed to deliver travoprost for 4-6 months



- 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 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, tolerability and pharmacodynamic profile of repeated dosing and multiple implants of OTX-TIC in beagle dogs.

METHODS

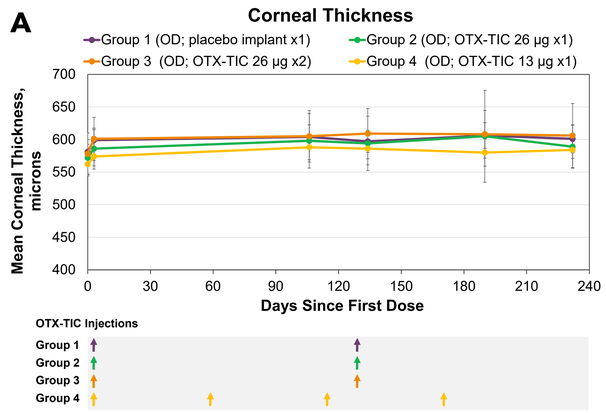
- OTX-TIC implant(s) containing different doses of travoprost were injected into the anterior chamber of the left eye in normotensive beagle dogs (Table 1)
  - Group 2 represents an intended clinical dose
  - Group 3 provides a 2X dose multiple and 2X implant safety factor for travoprost drug and implant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

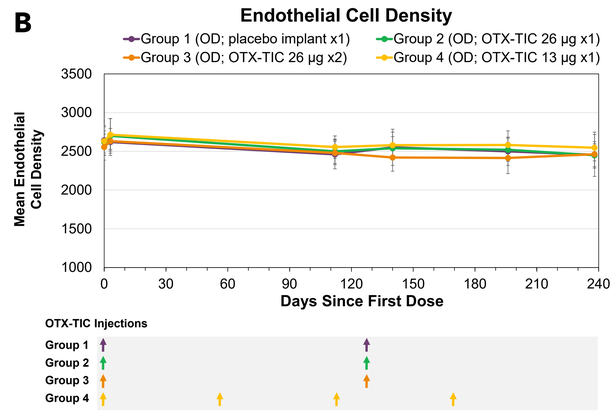
Group (n=8 animals/group)	Treatment		Dosing Frequency
	OD	OS	
1	One placebo implant	Two placebo implants	Q18W (Days 1 & 127)
2	One OTX-TIC 26 µg implants	Sham injection	Q18W (Days 1 & 127)
3	Two OTX-TIC 26 µg implants	None	Q18W (Days 1 & 127)
4	One OTX-TIC 13 µg implants	Sham injection	Q8W (Days 1, 57, 113, & 169)

- Ocular safety and tolerability following repeat dosing was evaluated by changes in corneal thickness (using ultrasound pachymeter), endothelial cell density (using noncontact specular microscopy), ocular exams and histopathology
- Intraocular pressure measurements were performed using rebound tonometer

RESULTS

- **No clinically meaningful effect of the active or placebo implants on corneal thickness and endothelial cell density was observed following repeat OTX-TIC dosing in any group, and no adverse ocular or systemic toxicity was observed.**



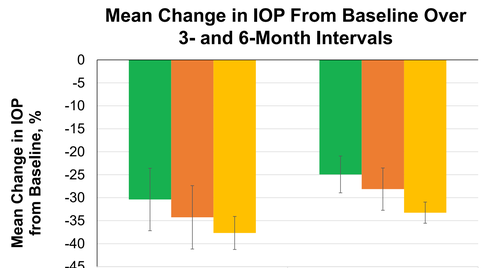


C

Assessments	Summary of Findings
Clinical Examinations	No findings considered OTX-TIC implant related
Ophthalmic Examinations	As expected for prostaglandin analogue agents in dogs, mild to moderate hyperemia (+1 to +2) and miosis (+3) were commonly observed throughout the study period in OTX-TIC eyes.
Systemic Exposure	Systemic exposure to travoprost following OTX-TIC dosing was low; all collected plasma samples being below the level of quantitation (2.00 ng/mL for travoprost and 0.100 ng/mL for travoprost acid)
Microscopic Observations	Histologic findings in all dosing groups were mild, non-adverse, and had no impact on the health of animals

- **Mean change in IOP demonstrated OTX-TIC had a sustained IOP lowering effect for at least 3-6 months and implants resorbed following each dosing.**

D



	3-Month (Day 0 through Day 78)	6-Month (Day 0 through Day 176)
Group 2 (26 ug x1 Q18W)	-30.38	-24.94
Group 3 (26 ug x2 Q18W)	-34.27	-28.13
Group 4 (13 ug x1 Q8W)	-37.67	-33.25

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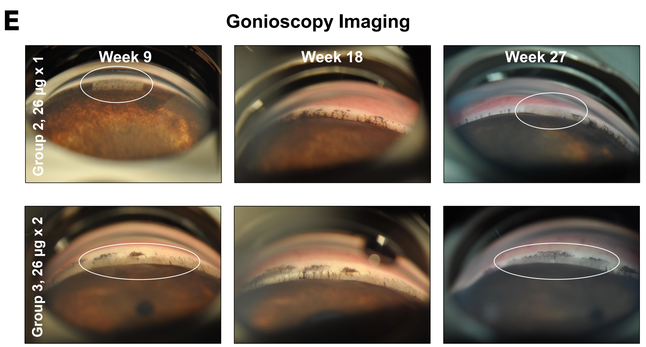

A. Corneal thickness measurements by ultrasound pachymeter; Error bars: SD. **B.** Endothelial cell density measured by noncontact specular microscopy; Error bars: SD. **C.** Summary of findings from ocular and systemic toxicity assessments **D.** Intraocular pressure lowering effect of multiple and repeated OTX-TIC doses in normotensive beagles; Error bars: SEM. **E.** OTX-TIC at Weeks 9, 18 and 27 in beagles, showing implant presence following initial dosing, absence and presence following repeat dosing, respectively, in animals receiving one vs. two 26 µg implants. Implants generally resorbed in the same time frame as the dosing interval.

CONCLUSIONS

- **Our data show that IOP lowering was sustained for at least 3-6 months and no safety concerns were observed following repeat dosing of OTX-TIC in beagle dogs.**
- **Multiple intracameral administrations of OTX-TIC implants were generally well tolerated in beagle dogs and did not result in clinically significant changes to the corneal endothelium.**
- **No-observed-adverse-effect levels (NOAELs) were considered to be 52µg/eye/dose administered at 18-week interval and 13µg/eye/dose administered four times at an 8-week interval.**
- **OTX-TIC 26µg implant is currently being evaluated for the treatment of open-angle glaucoma and ocular hypertension in a U.S. Phase 2 clinical trial.**

Presentation Disclosures: This poster discusses an investigational product; its efficacy and safety profile has not been established and it has not been approved by the U.S. Food and Drug Administration (FDA). **Funding**: These studies were funded by Ocular Therapeutix **Financial Disclosures**: All authors are employees of Ocular Therapeutix.

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.

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