A 6-Month GLP Toxicology Study of a Novel Hydrogel-based, Axitinib Intravitreal Implant (OTX-TKI) in Non-Human Primates

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BACKGROUND

- Neovascular retinal diseases may be responsive to tyrosine kinase inhibitors (TKIs) which have a broader anti-angiogenic profile than current standard-of-care VEGF agents[1-3] (**Figure 1**)
- OTX-TKI is a novel, hydrogel-based, biodegradable, intravitreal implant designed to deliver the potent tyrosine kinase inhibitor, axitinib, for up to 6-9 months for the treatment of neovascular retinal diseases (**Figure 2**)
- Previous studies have evaluated the safety and tolerability of OTX-TKI in rabbit and non-human models. In this study, we report the toxicity profile of of OTX-TKI in non-human primates.

Figure 1. Tyrosine Kinase Inhibitors Mechanism of Action

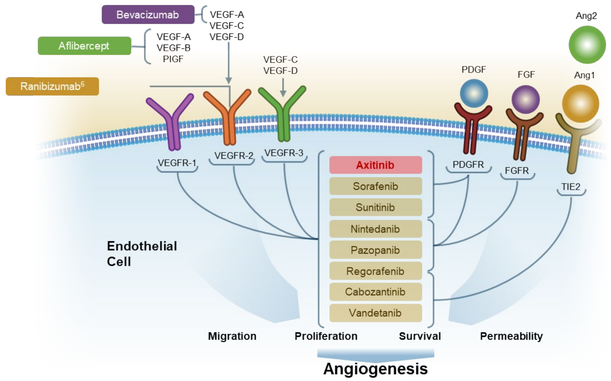
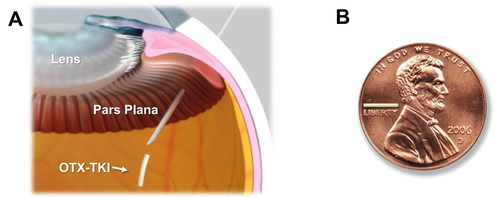


Figure 2. A) Schematic of OTX-TKI Injected into the Vitreous and B) Relative Size of Implant



STUDY OBJECTIVE

- **To evaluate the toxicological profile of axitinib intravitreal implant injection in Cynomolgus monkeys for a period of 6 months**

METHODS

- Six cynomolgus monkeys were injected intravitreally with an OTX-TKI 700 µg implant in the right eye and saline in the left eye (control)
  - OTX-TKI 700 µg dose represents a human equivalent dose of 1400 µg axitinib and 2.3X ocular dose safety margin when normalized to the vitreous volume between humans and monkeys
- Ophthalmic exams, IOP measurements, OCT images and confocal scanning laser ophthalmoscopy (cSLO) images were collected during the 6-month study

RESULTS

Figure 3. cSLO images show degradation of the insert over 6 months with no clinically significant changes in retinal morphology on corresponding OCT images

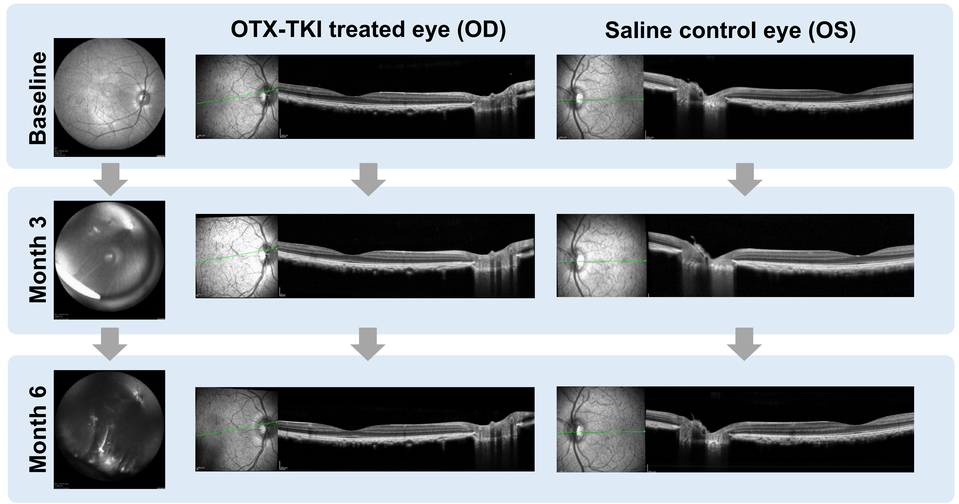
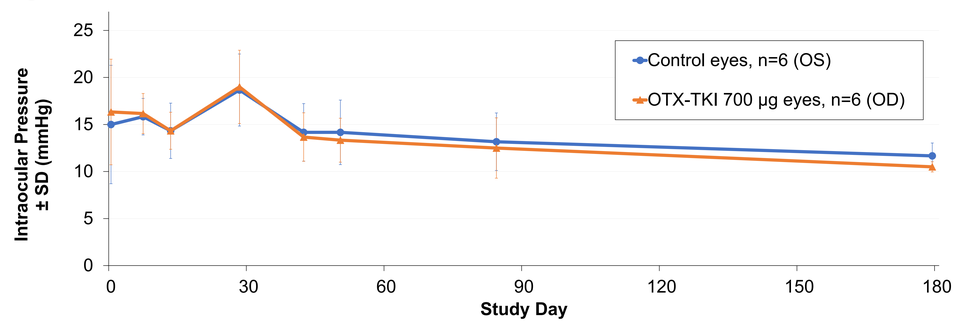


Figure 4. Intraocular Pressure



RESULTS (CON'T)

- No abnormalities were observed via ophthalmic exams and all ocular exam scores for vitreous cell & haze, and aqueous cell & haze were 0 through Month 6
- OCT imaging showed no clinically significant changes to retina morphology (**Figure 3)**
- Implants appeared idle and fully visible in the inferior vitreous to 5 months. At Month 6, cSLO images showed implants in a majority of animals (4/6) had completely degraded and the implants in the remaining two animals were beginning to degrade
- No statistically or clinically significant differences in IOP were observed between OTX-TKI and control eyes through 6-months (**Figure 4**)

CONCLUSIONS

- **No signs of inflammation or clinically significant changes in IOP were observed following intravitreal injection with OTX-TKI implant**
- **OTX-TKI degraded approximately at 6 months and no retinal abnormalities were observed**
- **Safety and efficacy of OTX-TKI 600 µg intravitreal implant is currently being evaluated in humans for the treatment of wet age-related macular degeneration in a U.S.-based Phase 1b study (NCT04989699)**

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

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Abbreviations: cSLO, confocal scanning laser ophthalmoscopy; IOP, intraocular pressure; OCT, optical coherence, tomography; SD, standard deviation; VEGF, vascular endothelial growth factor;

References: 1. Zhao Y, et al. *Oncologist*. 2015;20(6):660-673. **2.** Gross-Goupil M, et al. *Clin Med Insights Oncol*. 2013;7:269-277. **3.** Giddabasappa A, et al.. *Experimental Eye Research*. 2016;145:373-379.

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