Macular Volumetric Fluid Outcomes Following Intravitreal Axitinib Hydrogel Injection (OTX-TKI) in Non-Proliferative Diabetic Retinopathy

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PURPOSE

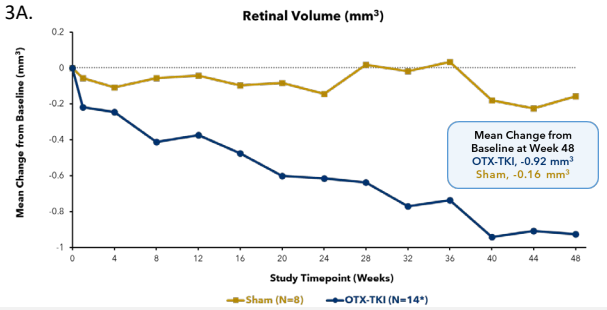
Moderately severe and severe non-proliferative diabetic retinopathy (NPDR) are chronic conditions that can progress to proliferative diabetic retinopathy, potentially causing vision impairment and blindness. Though previous randomized clinical trials have demonstrated early intervention with regular anti-vascular endothelial growth factor (VEGF) treatment mitigates disease progression, these treatments are often introduced at later stages.[1,2] Frequent intravitreal (IVT) anti-VEGF injections can be burdensome to patients, caregivers and providers, resulting in an unmet need for more durable treatment options designed to reduce burden. Administration of a single IVT injection of OTX-TKI in NPDR patients may provide for a reduction in treatment burden.

This study aimed to explore the effect of a single treatment with intravitreal axitinib hydrogel injection, OTX-TKI, on macular volume in non-proliferative diabetic retinopathy (NPDR).

RESULTS

- No patients in the study received rescue anti-VEGF injections
- OTX-TKI treated eyes consistently had greater reductions from baseline in mean retinal pigment epithelium volume between day 7 to week 48 compared to sham eyes
- OTKI-TKI treated eyes showed a consistent and sustained reduction in intraretinal fluid (IRF) from baseline, compared to a highly variable increase in IRF in sham-treated eyes
- Study limitations include small sample size and assuming observed effect is comparable to true effect

3A.



3B.

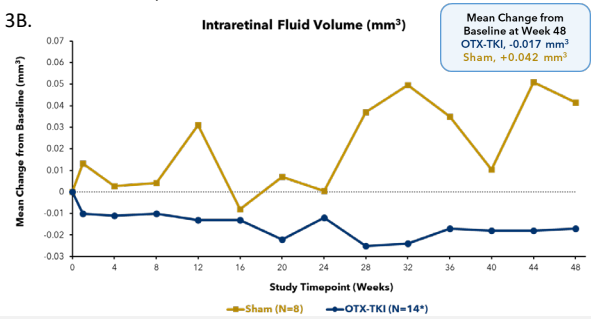
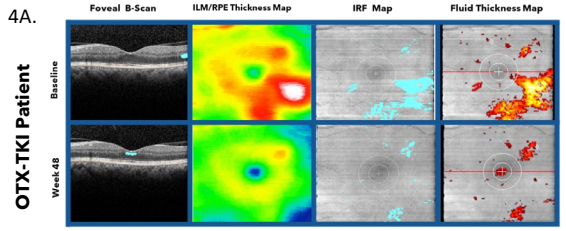


Figure 3. Mean retinal volume (mm³) (A) and (B) intraretinal fluid volume (mm³) (B) for randomized patients was monitored over the study period and measured every 4 weeks. *14 were enrolled, with one death unrelated to treatment prior to week 24 visit.

4A.



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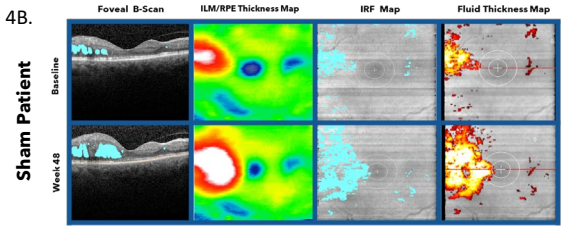

Figure 4. OCT scans from an OTX-TKI patient and a sham patient at week 0 (baseline) and week 48 of the study.

METHODS

OTX-TKI is an intravitreal hydrogel injection containing axitinib, a multitargeted tyrosine kinase inhibitor, that targets VEGF receptors. Axitinib has a high affinity for VEGFR2, a key driver of angiogenesis. OTX-TKI is injected as a single rod into the vitreous where it re-hydrates and then resorbs over 6 to 12 months (Figure 1).

Post-hoc analysis of the Phase 1 HELIOS trial, a randomized, controlled study comparing OTX-TKI to sham injection in NPDR patients (DRSS Level 43 or 57) without center-involved diabetic macular edema (CI-DME) (Figure 2). Spectral-domain OCT scans were read in a masked fashion using an automated, higher-order, machine-learning platform with certified reader validation and correction, as needed, to extract retinal volumetric measurements and retinal compartmental features.

1.

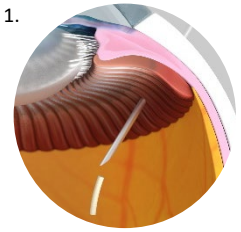

Figure 1. IVT injection of OTX-TKI. Image shown for illustrative purposes only.

2.

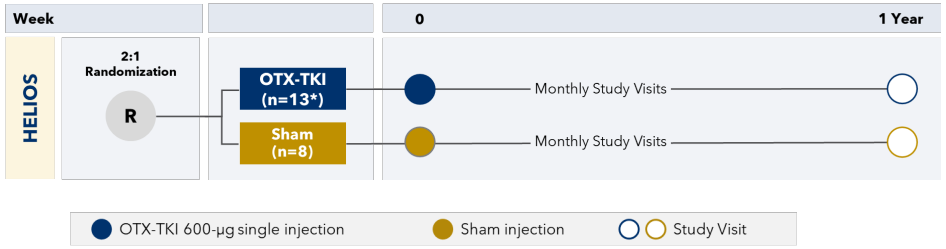

Figure 2. Patients randomized (2:1) were administered a single dose of either OTX-TKI or sham injections and monitored for 52 weeks. *14 were enrolled in the OTX-TKI arm, with one death unrelated to treatment prior to week 24 visit.

CONCLUSIONS

These results support the potential of OTX-TKI as a promising investigational treatment for diabetic retinopathy.

- Consistent improvement in fluid metrics and macular volume was observed in OTX-TKI-treated patients compared to sham
- These findings complement the primary analysis of HELIOS, which showed OTX-TKI was generally well tolerated with no incidence of treatment or injection procedure-related intraocular inflammation, DRSS stability or improvement with durability through 48 weeks and no OTX-TKI patients developed PDR or CI-DME through week 48

Support: This study was sponsored by Ocular Therapeutix. **Presentation Disclosures:** The following presentation discusses an investigational drug, OTX-TKI, in development. OTX-TKI's efficacy and safety profiles have not been established, and it has not been approved for marketing by the FDA or any other health agency. This study was conducted in accordance with the U.S. Department of Health and Human Services, Food and Drug Administration, United States Code of Federal Regulations. **Author Disclosures:** Amy Tang: None; Reem Amine: None; Lyndsey Della Vecchia: None; Neal Shah: None; John Mamone: None; Erin Flannigan: None; Penina Schlesinger: None; Jasmine Scafuro: None; Julia Beilis: None; Michelle Bonnay: None; Karissa Zarbock: None; Barret Schmidt: None; Jamie Reese: None; Sunil Srivastava: None; Justis Ehlers: Code C (Consultant/Advisor).

References: 1. Maturi *et al. JAMA* 2023 Feb 7;329(5):376-385. **2.** Brown *et al. JAMA Ophthalmol* 2021 Sept 1;139(9):946-955.