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

Devesh Kumar[1], Amy Tang[1], Reem Amine[1], Lyndsey Della Vecchia[1], Neal Shah[1], John Mamone[1], Erin Flannigan[1], Penina Schlesinger[1], Jasmine Scafuro[1], Julia Beilis[1], Michelle Bonnay[1], Karissa Zarbock[1], Barret Schmidt[1], Jamie Reese[1], Sunil K. Srivastava[1] and Justis P. Ehlers[1]

[1]Cole Eye Clinic at Cleveland Clinic, Cleveland, OH, United States.

Objective

- To explore the effect of a single treatment with intravitreal axitinib hydrogel injection, OTX-TKI, on macular volume in non-proliferative diabetic retinopathy.

Purpose

- Assessing compartmental fluid dynamics in diabetic retinopathy may provide a more precise understanding of disease progression, treatment response, and potential biomarkers for therapy optimization.

Conclusions

- OTX-TKI patients compared to sham demonstrated evidence of consistent improvement in fluid metrics and macular volume over the study period.
- These findings complement the primary analysis of HELIOS; OTX-TKI was generally well tolerated with no incidence of treatment or injection procedure-related intraocular inflammation. OTX-TKI-treated patients had stable or improved DRSS scores and did not developed PDR or CI-DME through Week 48.

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

Financial Disclosures

Devesh Kumar: None; 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 K. Srivastava: None; Justis P. Ehlers: Consultant: Novartis, Zeiss, Leica, Beyeonics, Alcon, Allergan, Adverum, Oxurion, Roche, Allegro, Abbvie, Stealth, RegenxBIO, Iveric Bio, Boerhinger-Ingelheim, Apellis, Exegenesis, Astellas, Ocular Therapeutix, Perceive Biotherapeutics, and Regeneron. Grant Support: Novartis, Zeiss, Alcon, Abbvie, Allergan, Adverum, Oxurion, Perceive Biotherapeutics, Roche, Stealth, Iveric Bio, Ocular Therapeutix, and Regeneron.

Study and Product Disclosures

This study was sponsored by Ocular Therapeutix. 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.

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.

Presented at the 43rd Annual Scientific Meeting of the American Society of Retina Specialists | July 30th – August 2nd, 2025

Background/Introduction

- Moderately severe and severe non-proliferative diabetic retinopathy (NPDR) are chronic conditions that can progress to proliferative diabetic retinopathy or central-involved diabetic macular edema, 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 a reduction in treatment burden.

Methods

- OTX-TKI is an intravitreal hydrogel incorporating axitinib, a small molecule, multi-target, tyrosine kinase inhibitor (TKI) with angiogenic properties. OTX-TKI is injected as a single rod into the vitreous that hydrates and then resorbs over 6 to 12 months (Figure 1).
- Post-hoc analysis of the Phase 1 HELIOS trial, a randomized, controlled study compared OTX-TKI to sham injection in moderately severe to severe NPDR patients Diabetic Retinopathy Severity Scale (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.

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

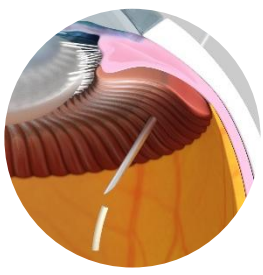
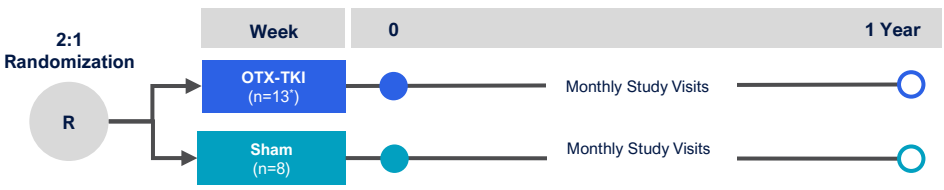


Figure 2. Patients randomized (2:1) were administered a single dose of either OTX-TKI or sham injections and monitored for 1 year.



*14 patients were enrolled in the OTX-TKI arm, with one death unrelated to treatment prior to week 24 visit.

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 (Figure 3a)
- 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 (Figure 3b)
- Study limitations include small sample size and assuming observed effect is comparable to true effect.

Figure 3A.

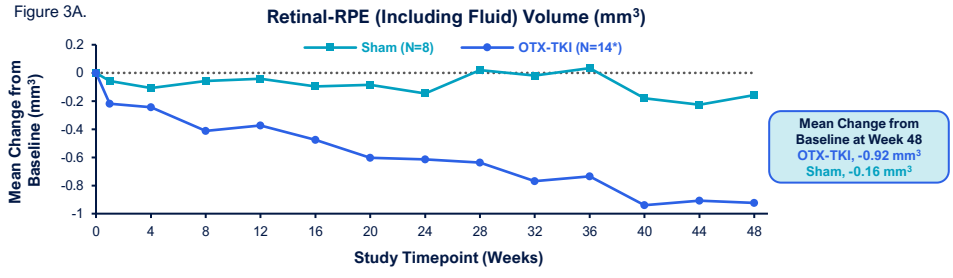
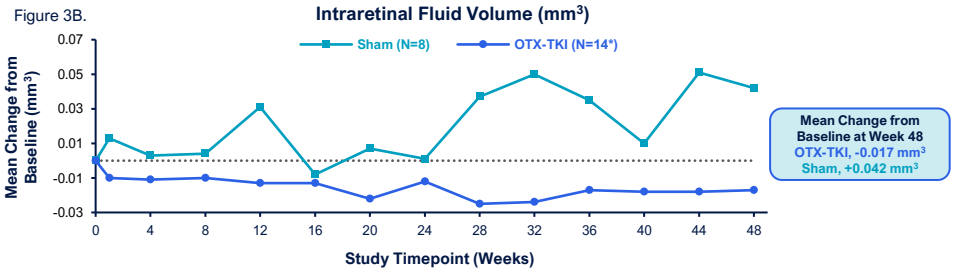


Figure 3B.



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

Figure 4A.

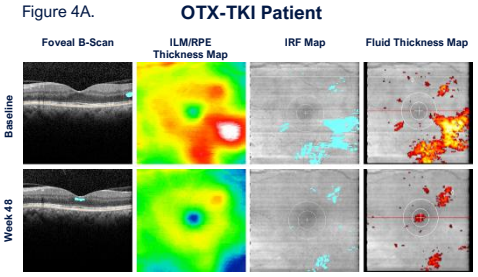
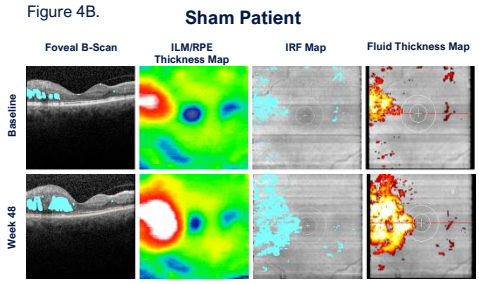


Figure 4B.



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