Macular Fluid Volumetric Outcomes Following a Single Axitinib Intravitreal Hydrogel (OTX-TKI) from the HELIOS Clinical Trial for Diabetic Retinopathy

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On Behalf of the HELIOS Study Investigators

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EURetina 2025 | Paris, France | September 4-7, 2025

Disclosures and Acknowledgements

Presenter Disclosures (Margaret Chang, MD, MS)

Speaker: Genentech

Consultant: Genentech, AbbVie/RegenXBio, Astellas, Zeiss, Ocular Therapeutix, Opthea, Oculis, Eyepoint, Boerhinger, Ollin, Outlook

Research support: Novartis, NGM, Eyebio, OcuTerra, Alexion, Mylan, Outlook, Kodiak

Stock Options: Ollin

Study 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 U.S. Food and Drug Administration (FDA) or any other health agency.

Funding was provided by Ocular Therapeutix for the study.

Acknowledgments

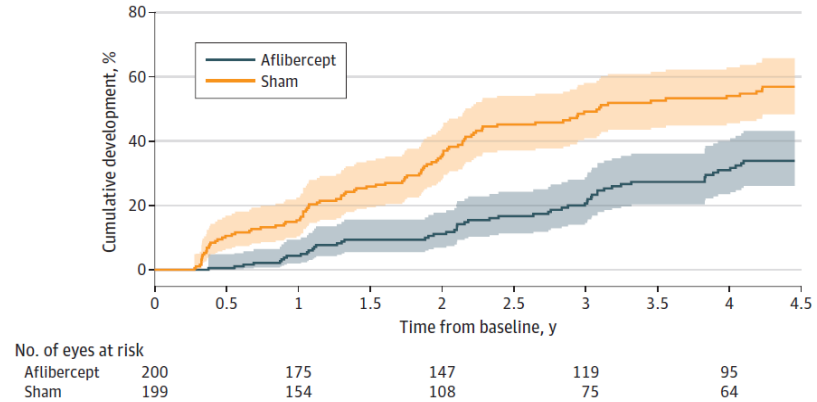
OCT Analysis based on the findings of Justis P. Ehlers, MD, and his Cole Eye research team (2025).

Introduction: Efficacy of Anti-VEGF in Diabetic Retinopathy is Established, Earlier Treatment to Prevent Progression is Needed

- Moderately severe and severe non-proliferative diabetic retinopathy are chronic conditions that can progress to proliferative diabetic retinopathy (PDR) or central-involved diabetic macular edema (CI-DME), 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]

PANORAMA STUDY

Cumulative Development of PDR or CI-DME with Vision Loss[1]



Early intervention prevents progression to severe or vision-threatening disease

American Society of Retina Specialists

2023 PREFERENCE AND TRENDS SURVEY[2]

62.3%

of international retinal specialists **do not recommend anti-VEGF therapy** for NPDR without DME

Despite established efficacy and safety, **<1% of NPDR patients are treated** with anti-VEGF therapy[3,4]

- 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 prevent vision threatening complications.

References: 1. Maturi RK, et al. *JAMA.* 2023;329(5):376-385. 2. Hahn P, Garg SJ, eds. 2023 Global Trends in Retina Survey. Chicago, IL. American Society of Retina Specialists; 2023. 3. Market Scope. 2022 Retinal Pharmaceuticals Market Report: Global Analysis for 2021 to 2027. Published August 2022. 4. Market Scope. US Retina Quarterly Update: Q2 2022 Analysis of Historical Trends and Latest Developments. Published August 2022

Materials and Methods: Phase 1 HELIOS Trial & Post-Hoc Analysis

- 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 hydrogel into the vitreous that hydrates and then resorbs over 6 to 12 months (Figure 1).
- The Phase 1 HELIOS trial, a randomized, controlled study compared 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.

Figure 1.

Figure 2.

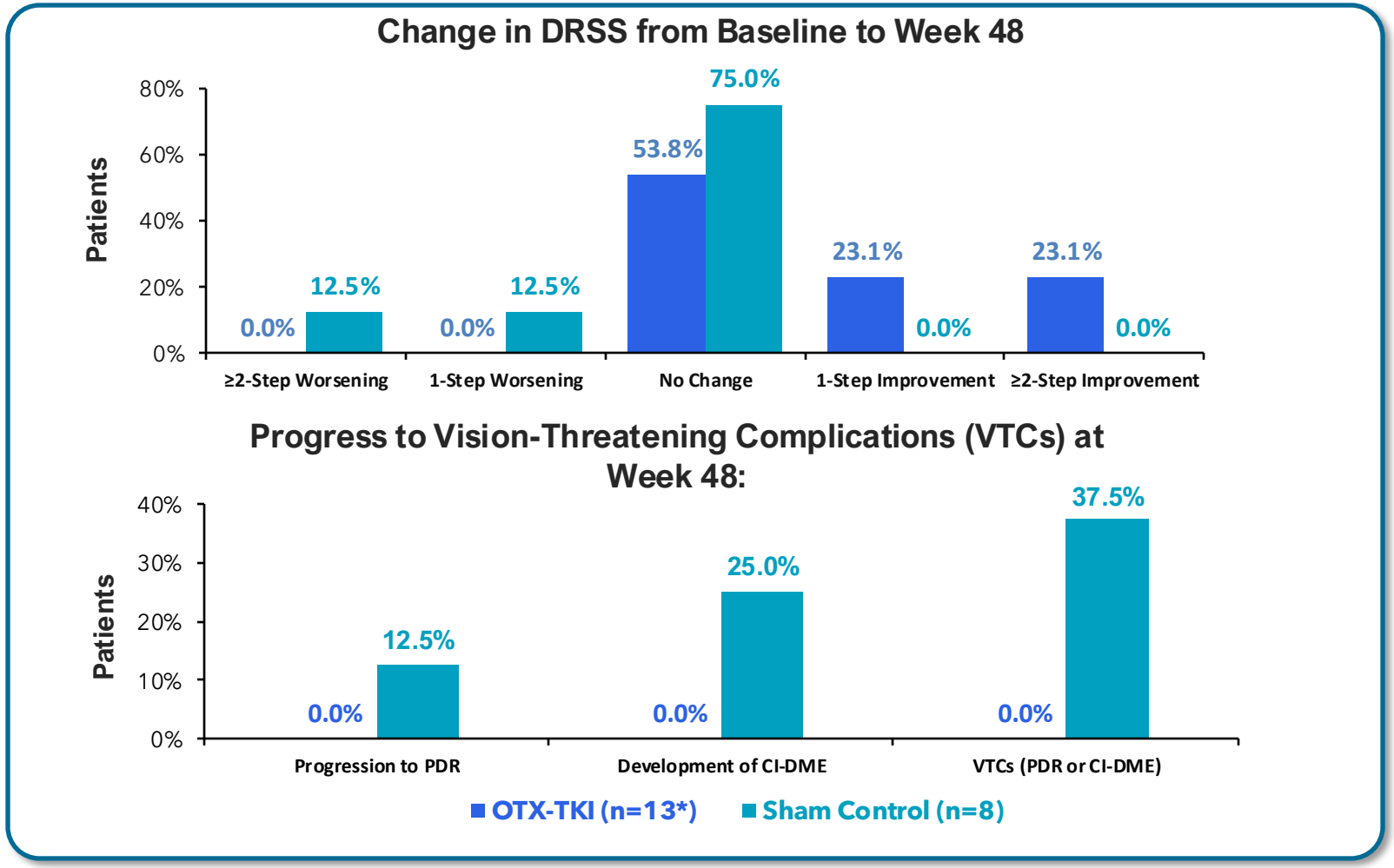
Figure 1. IVT injection of OTX-TKI. Image shown for illustrative purposes only. Figure 2. Patients randomized (2:1) were administered a single dose of either OTX-TKI or sham injections and monitored for 1 year. *14 were enrolled in the OTX-TKI arm, with one death unrelated to treatment prior to week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

Non-Proliferative Diabetic Retinopathy (NPDR), Diabetic Retinopathy Severity Score (DRSS), Optical Coherence Tomography (OCT)

Phase 1 Study Demonstrates at Week 48, More OTX-TKI Patients had DRSS Improvement and Did Not Develop Vision-Threatening Complications Compared to Sham

Safety Summary

- All AEs were mild and balanced across the two arms, with no moderate or severe AEs reported in either arm
- No ocular SAEs reported in either arm
- No treatment- or injection procedure-related intraocular inflammation, iritis, vitritis, or vasculitis
- No subjects in either arm received rescue medication



*14 were enrolled, with one patient death unrelated to treatment prior to week 24 visit

Abbreviations: DRSS (Diabetic retinopathy severity scale); CI-DME (Center-involved diabetic macular edema); PDR (Proliferative diabetic retinopathy); VTC (vision-threatening complications [includes PDR or CI-DME]); AE (adverse event); SAE (serious AE). https://www.ophthalmologytimes.com/view/1-year-results-from-helios-trial-show-stability-or-improvement-in-treating-npdr

Results: Consistent Improvement in Fluid Metrics Was Observed in OTX-TKI Patients Compared to Sham

Figure 3A.

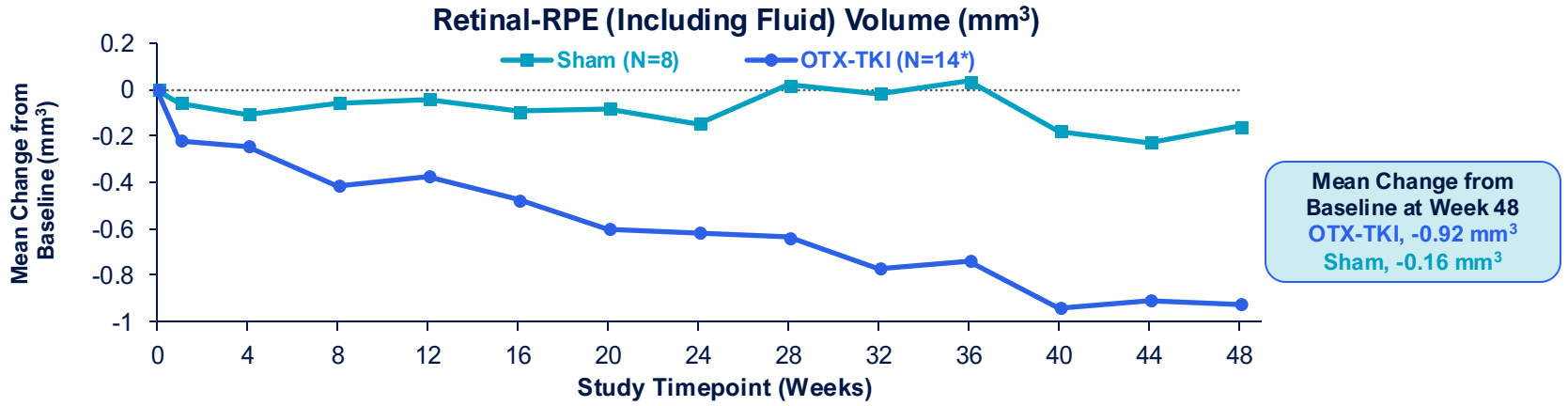
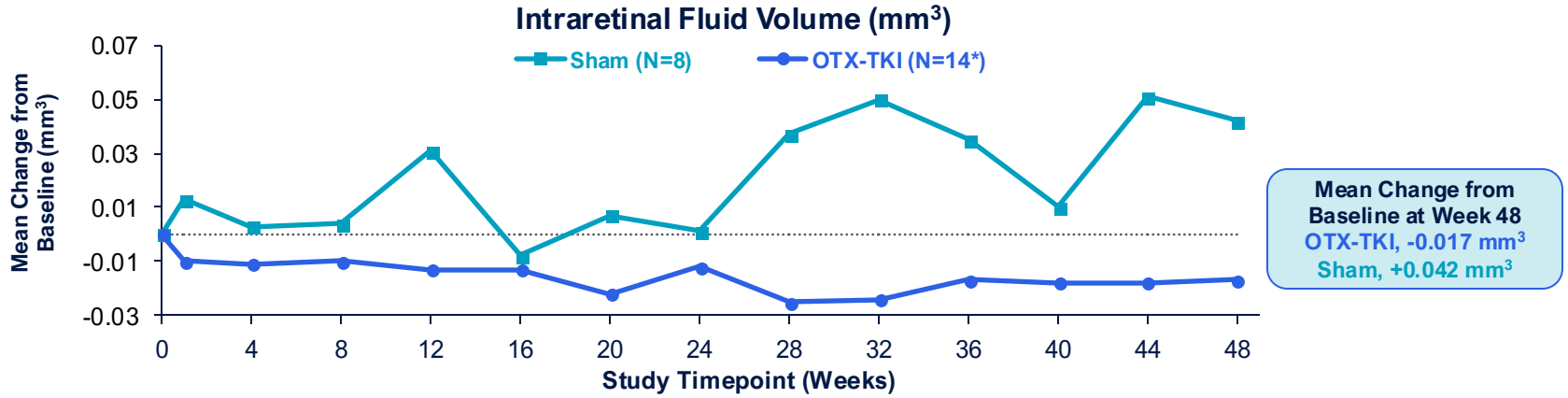


Figure 3B.



- 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).
- OTX-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 3. Mean change from baseline in retinal volume (mm^3) (A) and (B) intraretinal fluid volume (mm^3) 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

Vascular Endothelial Growth Factor (VEGF), Retinal Pigment Epithelium (RPE)

Results: Multi-Layer OCT Analysis Demonstrates Reduction in Fluid in OTX-TKI Patient Compared to an Increase in Sham Patient Over 48 Week Period

Figure 4A.

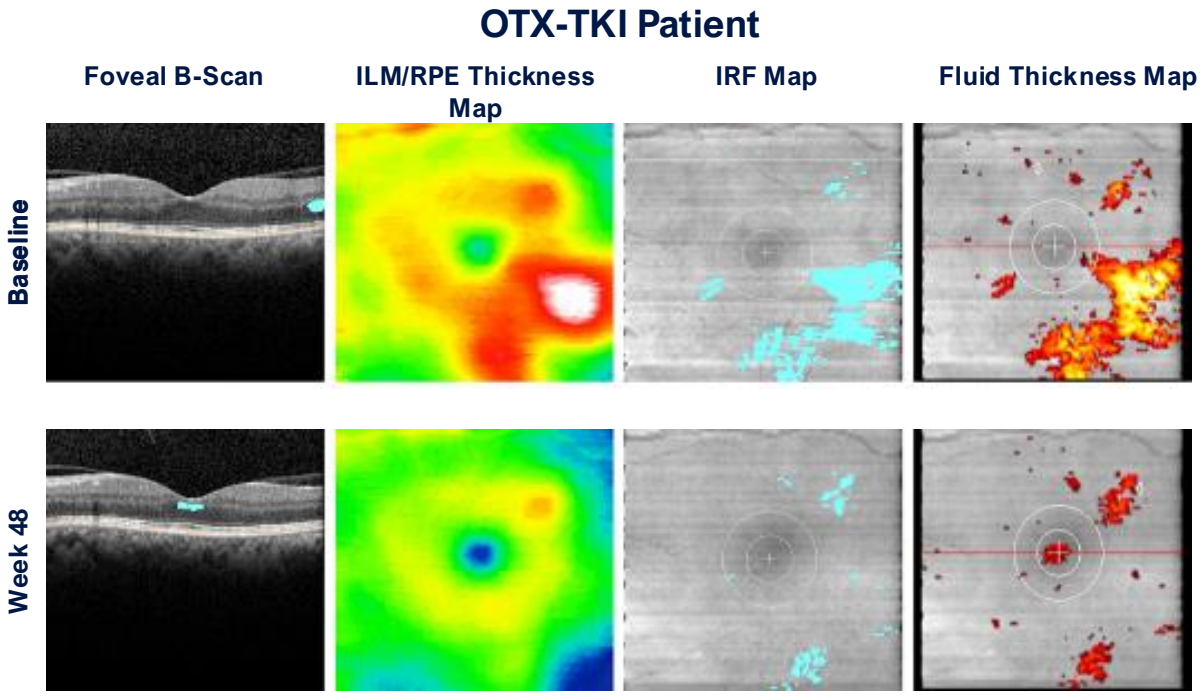


Figure 4B.

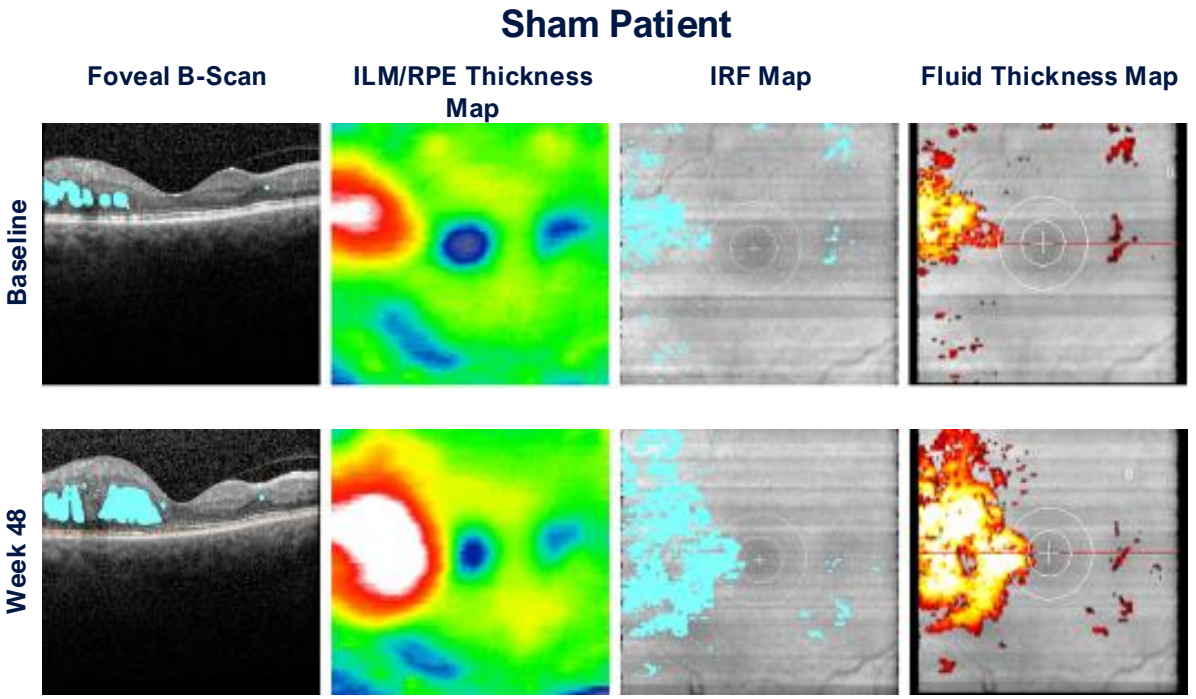


Figure 4. OCT scans from an OTX-TKI patient (A) and a sham patient (B) at week 0 (baseline) and week 48 of the study.

Inner Limiting Membrane (ILM), Retinal Pigment Epithelium (RPE), Intraretinal Fluid (IRF)

Conclusions: Quantitative Analysis of Macular Fluid Volumes in Phase 1 HELIOS Trial

- 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 develop a vision threatening complication, PDR or CI-DME, through Week 48.

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

Diabetic Retinopathy Severity Score (DRSS), Proliferative Diabetic Retinopathy (PDR), Central-Involved Diabetic Macular Edema (CI-DME)