

Longitudinal Quantitative Ultra-Widefield Retinal Leakage Assessment in Diabetic Retinopathy Following a Single Axitinib Hydrogel (OTX-TKI) in the HELIOS Trial

Katherine E. Talcott, MD¹

talcotk@ccf.org

Reem Amine¹; Amy Tang¹; Lyndsey Della Vecchia¹; Erin Flannigan¹; Penina B. Schlesinger¹; Jasmine Scafuro¹; Julia L. Beilis¹; Michelle Bonnay¹; Karissa Zarbock¹; Jamie Reese¹; Sunil K. Srivastava, MD¹; Justis P. Ehlers, MD¹

On Behalf of the HELIOS Study Investigators

¹ Cleveland Clinic, Cleveland, OH, United States.

Disclosures

Presenter Disclosures (Katherine Talcott, MD)

4DMT (consultant), Alimera (consultant), Abbvie (consultant), Apellis (consultant), Astellas (speaker's bureau), Bausch and Lomb (consultant), Eyepoint (consultant), Genentech (consultant, speaker's bureau), Harrow (consultant), Ocular Therapeutics (consultant), Outlook (consultant), Regeneron (consultant, research), Zeiss (consultant, research, speaker)

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.

OTX-TKI: Sustained-Release Axitinib in Hydrogel



ELUTYX TECHNOLOGY

Bioresorbable, Targeted, Sustained Drug Delivery

- Proprietary bioresorbable polymer matrix is a hydrogel-based, versatile, biocompatible platform for localized sustained drug delivery

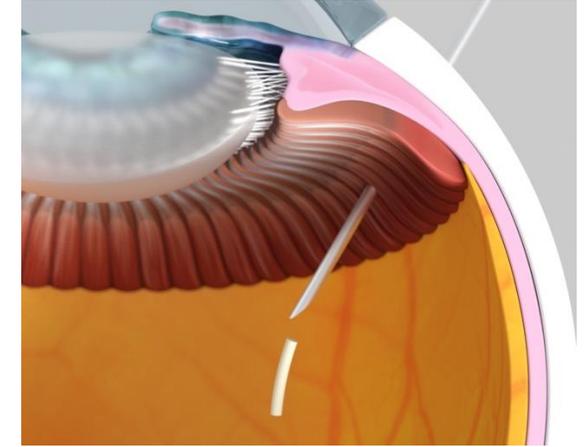
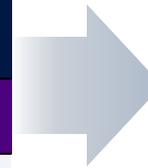


Drug	Inhibitory Concentrations for VEGFR2/KDR (Kinase Domain Receptor) in nM (Lower Inhibitory Concentration-50 values indicate higher affinity)
Axitinib ⁵	0.2
Sunitinib ⁶	40
Vorolanib ⁶	64

AXITINIB

Multi-target Tyrosine Kinase Inhibitor

- ~100X more potent for VEGFR-2 compared to sunitinib and vorolanib¹⁻³
- Highly selective for all VEGF receptors⁴⁻⁶ with no TIE2 inhibition at physiologic tissue concentrations¹



OTX-TKI

Single Intravitreal Bioresorbable Hydrogel Injection

- Sustained axitinib release expected to allow for a redosing interval for 6-12 months
- Administered by a 25G needle

Abbreviations: IC (inhibitory concentration); KDR (kinase domain receptor); TIE2 (Tyrosine kinase with immunoglobulin-like and EGF-like domains-2); TKI (Tyrosine kinase inhibitor); VEGF (Vascular endothelial growth factor [receptor]).

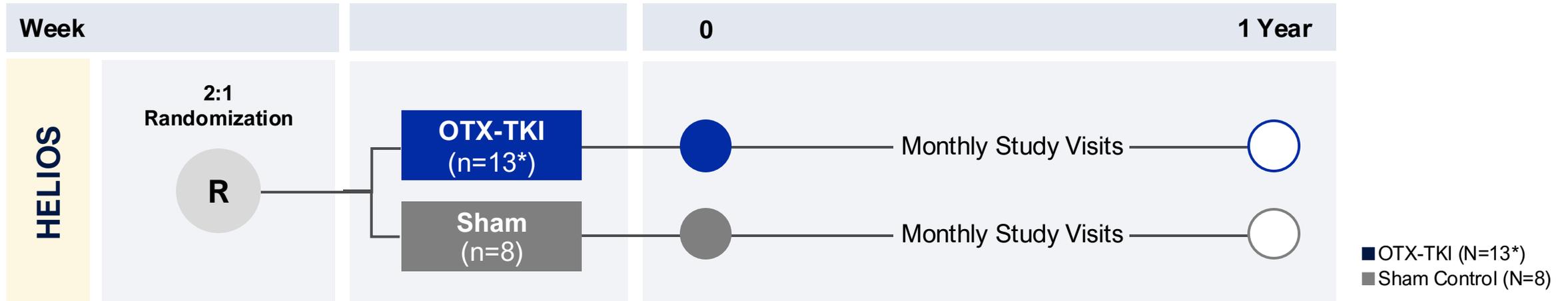
References: 1. Unpublished data; Data on File. 2. Hu-Lowe DD, et al. Clin Cancer Res. 2008;14(22):7272-7283. 3. McTigue M, et al. Proc Natl Acad Sci U S A. 2012;109(45):18281-18289. 4. Zhao Y, et al. Oncologist. 2015;20(6):660-673. 5. Gross-Goupil M, et al. Clin Med Insights Oncol. 2013;7:269-277. 6. Liang C, et al. Mol Ther Oncolytics. 2022;24:577-584.

HELIOS Phase 1 Study of OTX-TKI in NPDR

DESIGN

Multi-center, double-masked, randomized, parallel group study of OTX-TKI in moderately-severe to severe NPDR without CI-DME.

TRIAL SCHEMATIC



STUDY OUTCOMES

PRIMARY: Safety and tolerability of OTX-TKI

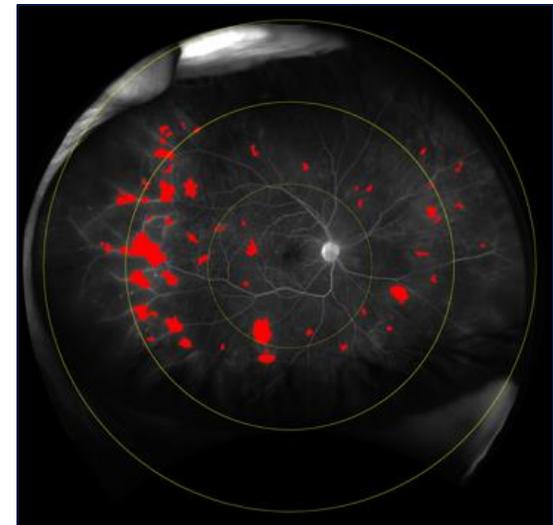
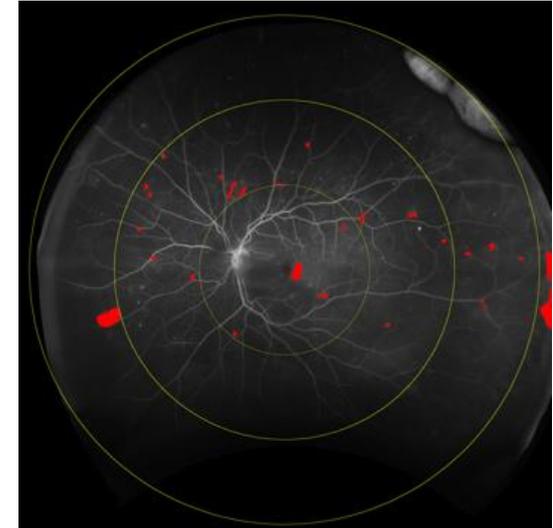
SECONDARY: DRSS changes, rescue therapy, BCVA, and CSFT changes

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

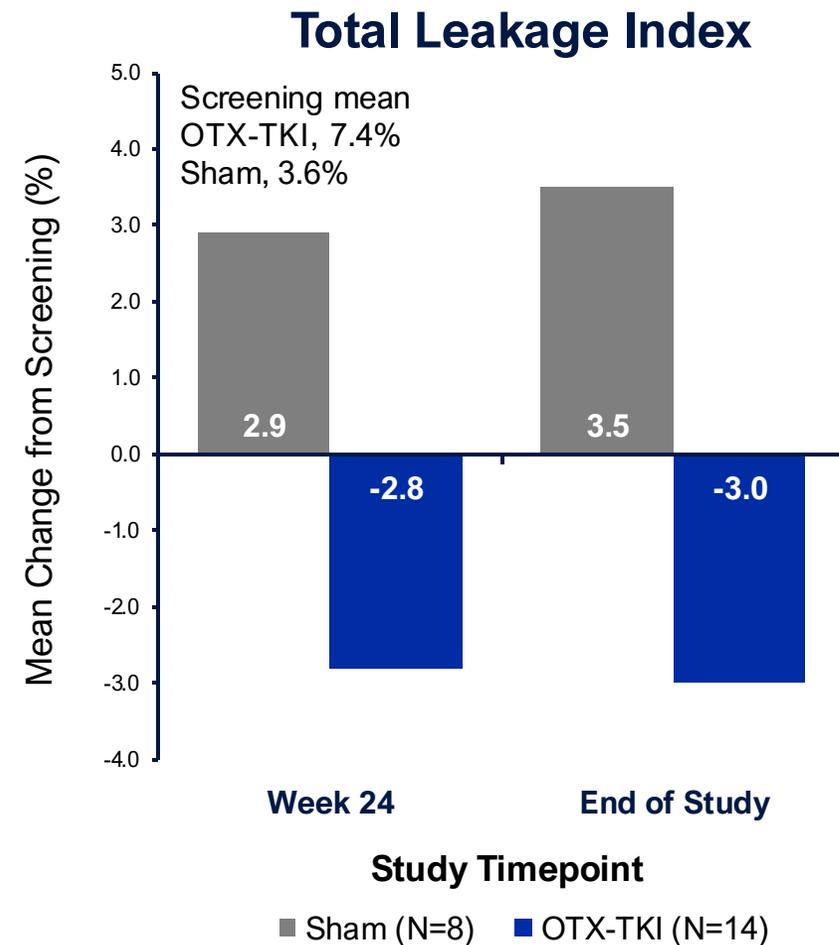
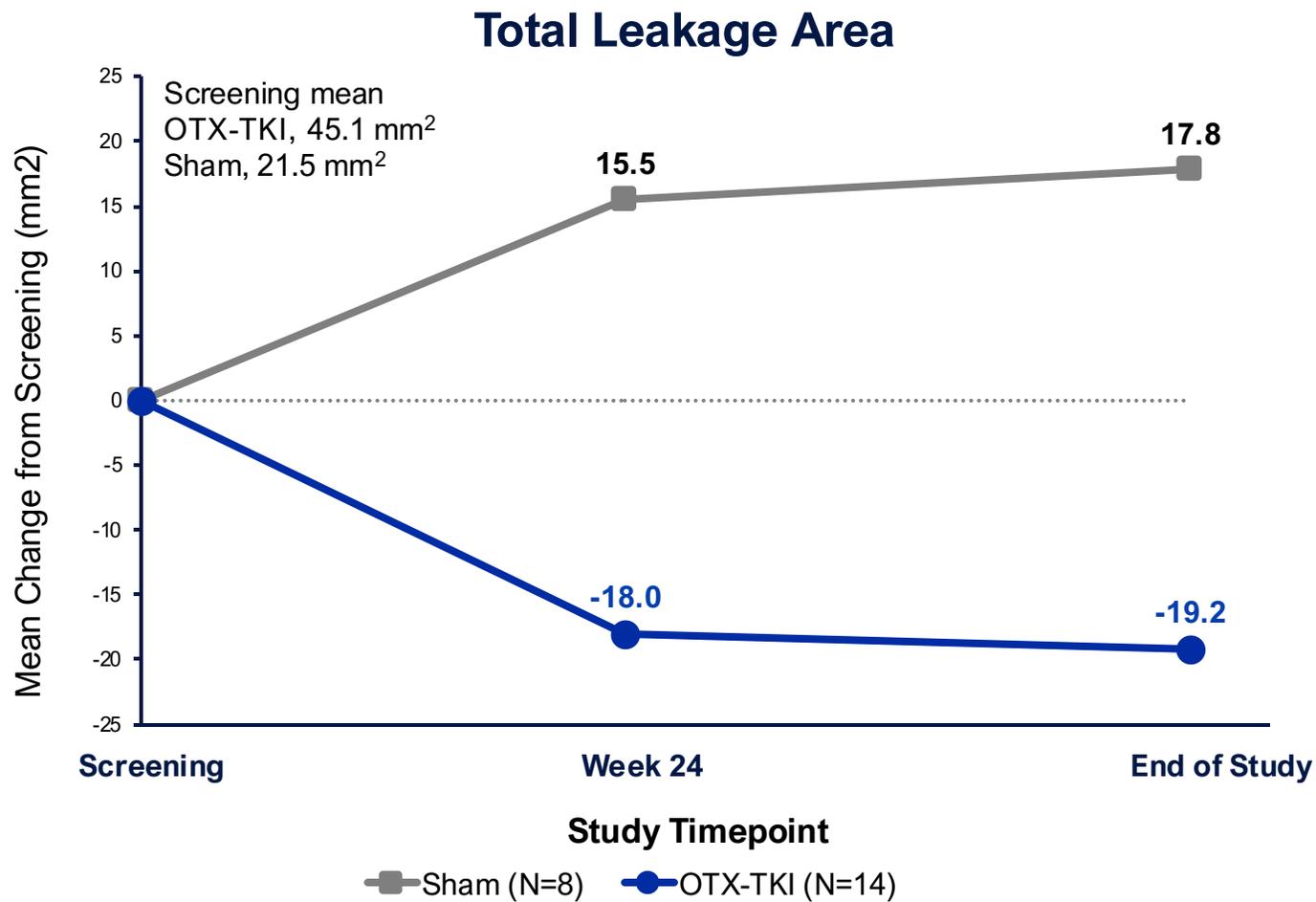
Abbreviations: BCVA (Best-corrected visual acuity); CI-DME (Center-involved diabetic macular edema); CSFT (Central subfield thickness); DRSS (Diabetic retinopathy severity scale); NPDR (Non-proliferative diabetic retinopathy).

Ultra Widefield Fluorescein Angiography Quantitative Leakage Analysis

- Masked longitudinal assessment of quantitative leakage on UWFA images was conducted using a machine-learning augmented feature extraction platform.
- Leakage index was calculated as the proportion of retinal leakage (ie, hyperfluorescence) within the analyzable retina area.
- Leakage segmentation validation was performed by certified readers with correction, as needed.

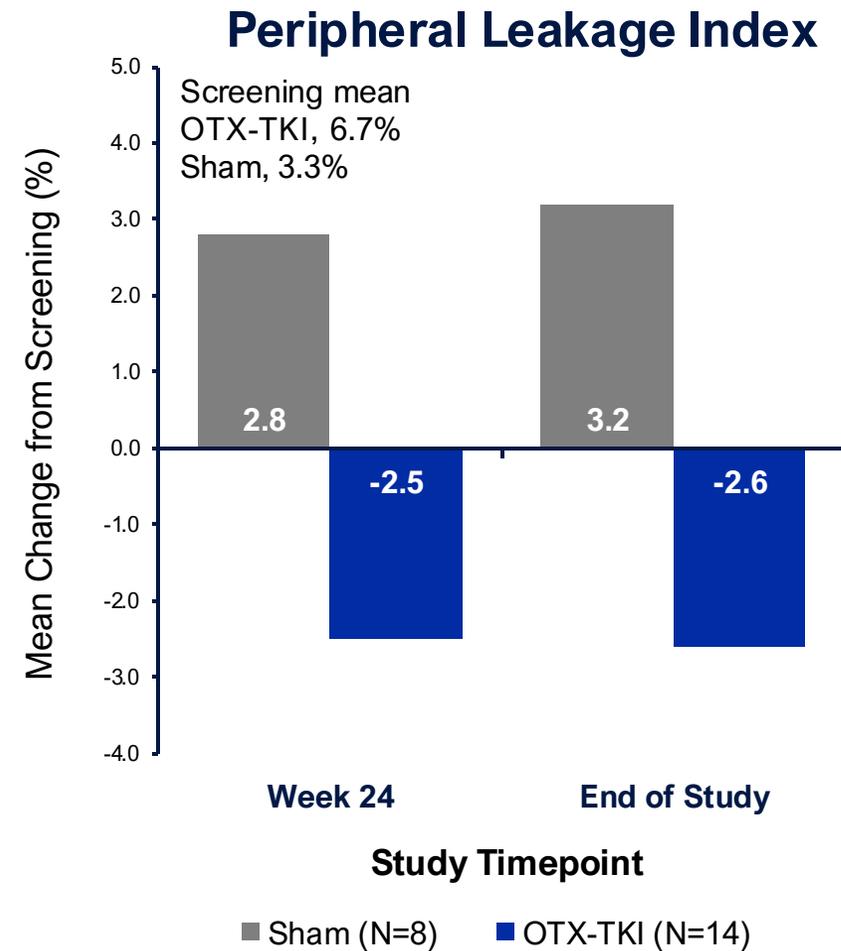
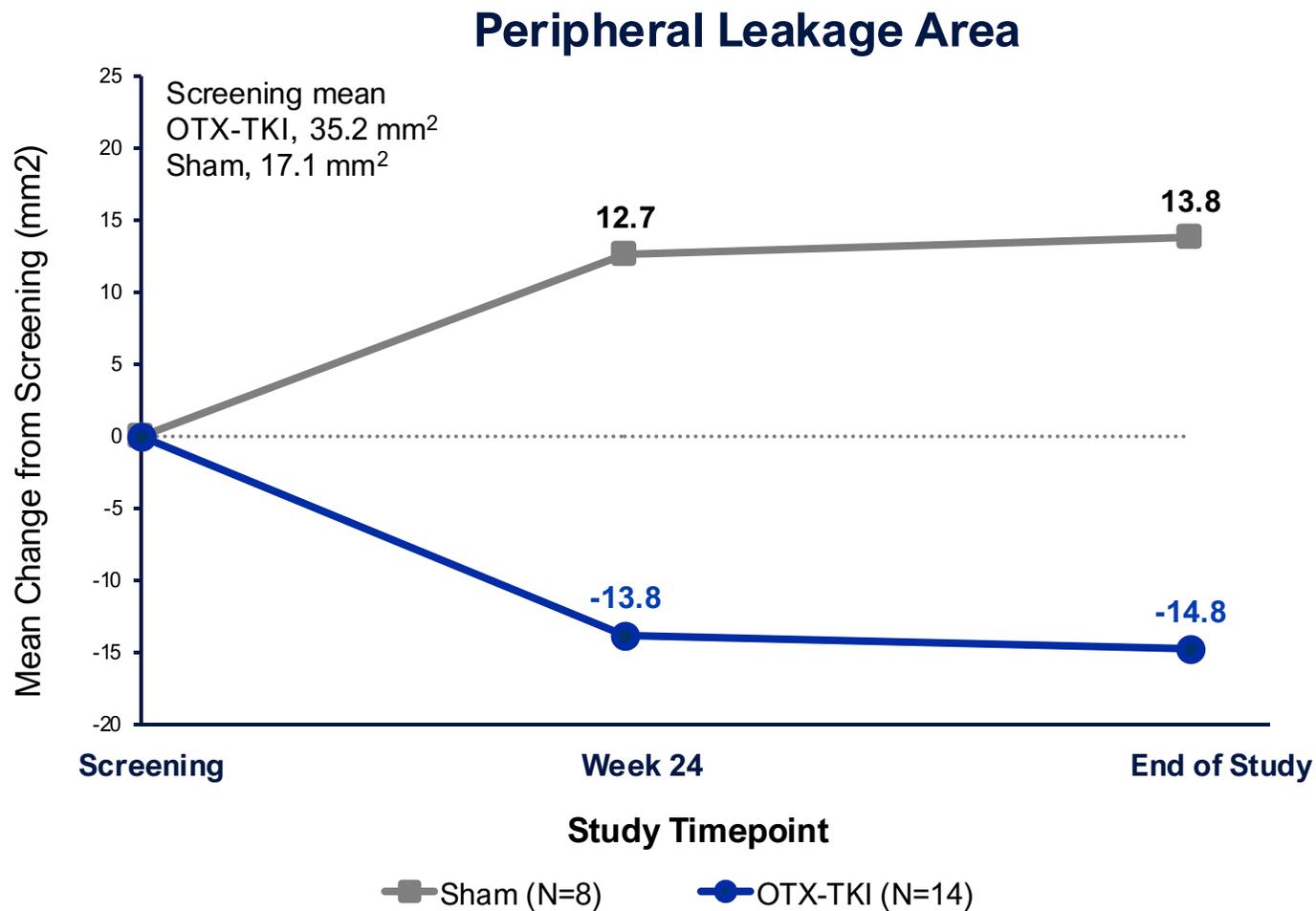


Durable Reduction in Total Retinal Vascular Leakage Across One Year Observed with OTX-TKI Compared to Sham



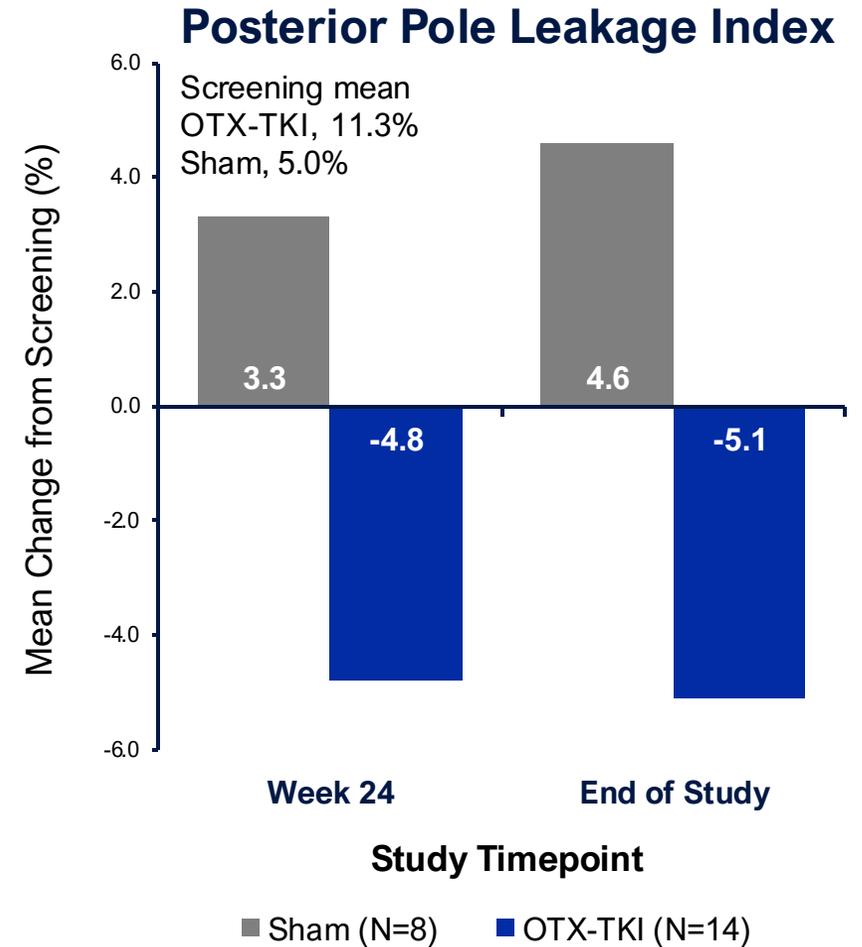
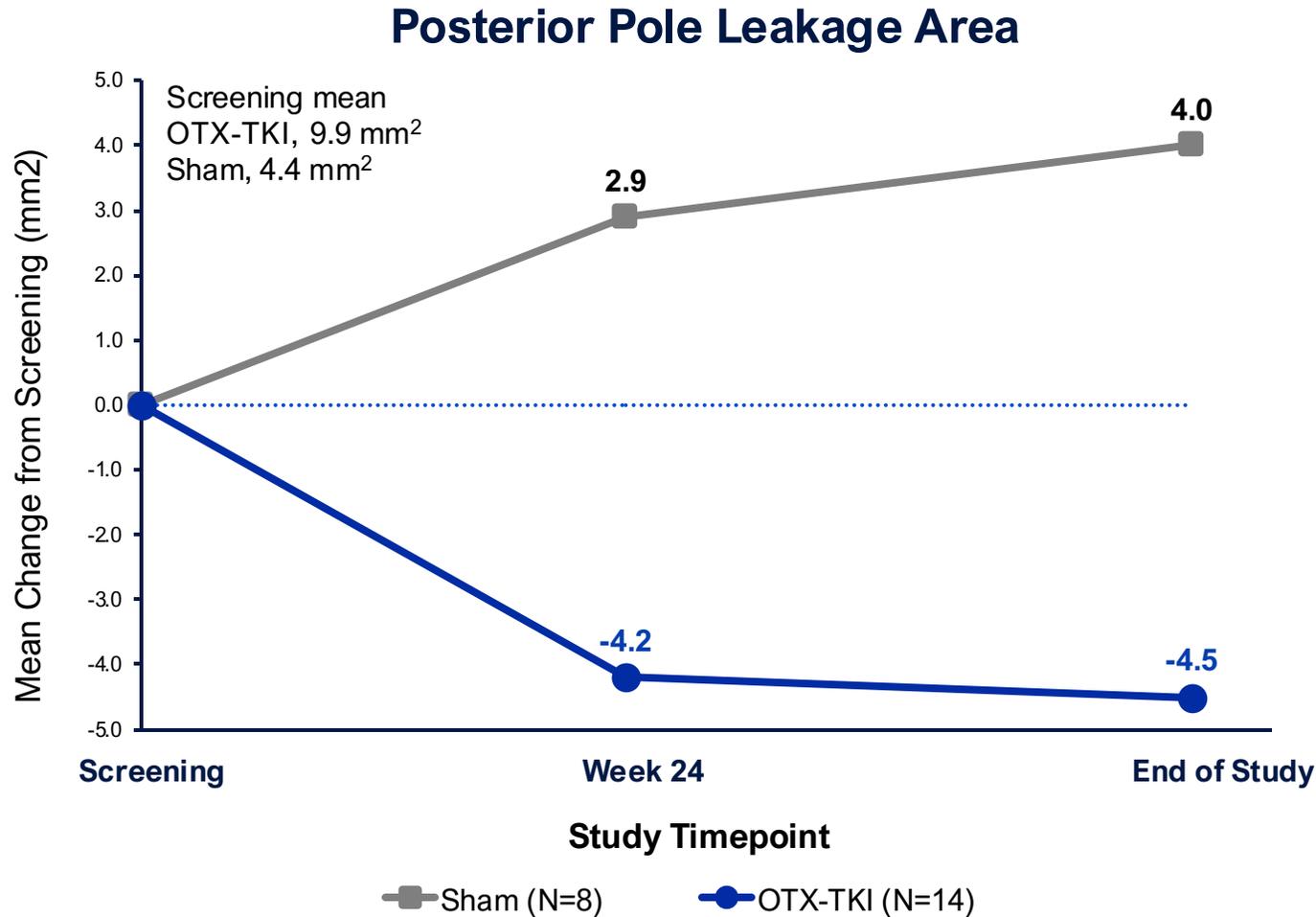
*14 patients enrolled in OTX-TKI treatment arm, with 1 patient death unrelated to treatment.

Peripheral Leakage Parameters Improved in OTX-TKI Eyes, While Worsening Was Observed in Sham Eyes



*14 patients enrolled in OTX-TKI treatment arm, with 1 patient death unrelated to treatment.

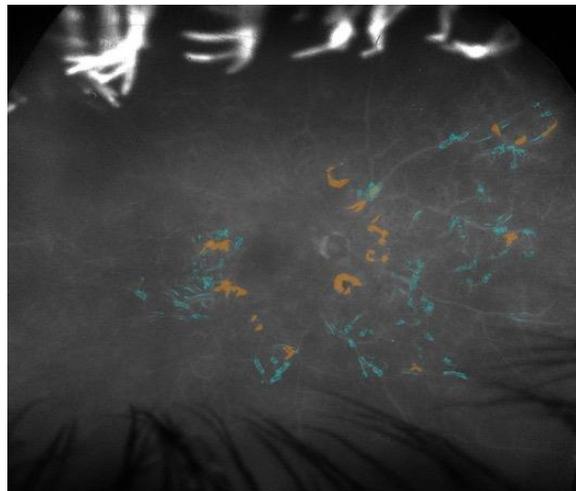
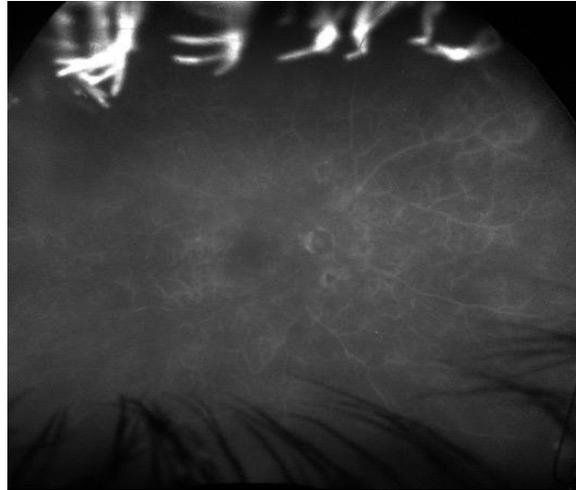
OTX-TKI Eyes Show Sustained Reduction in Leakage Parameters Across Posterior Pole



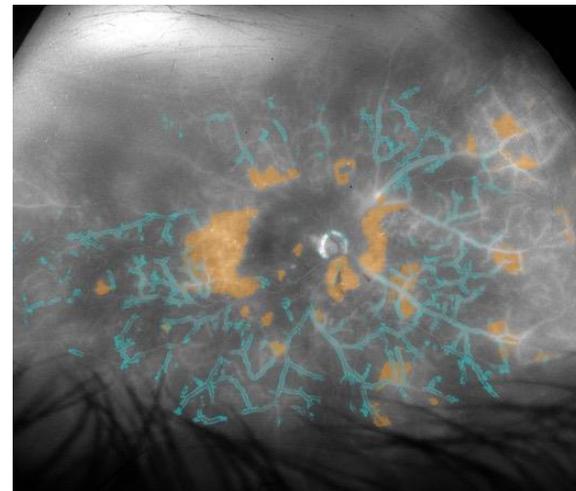
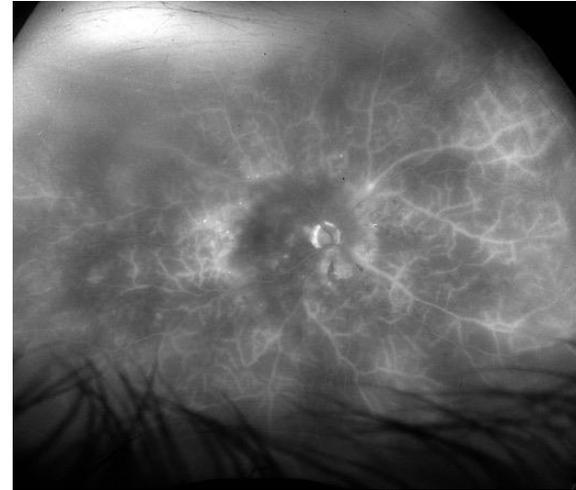
*14 patients enrolled in OTX-TKI treatment arm, with 1 patient death unrelated to treatment.

Case Example: Sham Patient

BASELINE

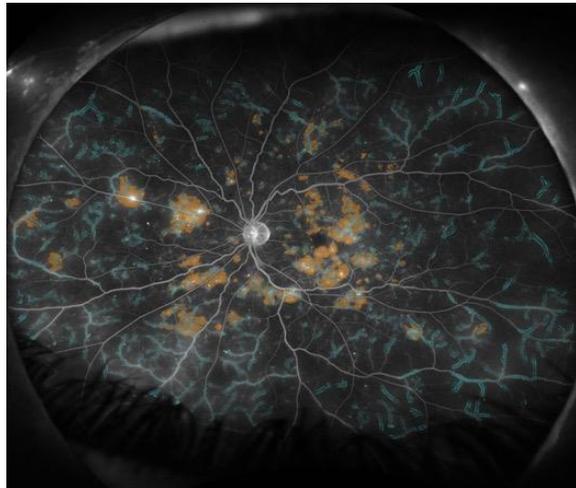


END OF STUDY

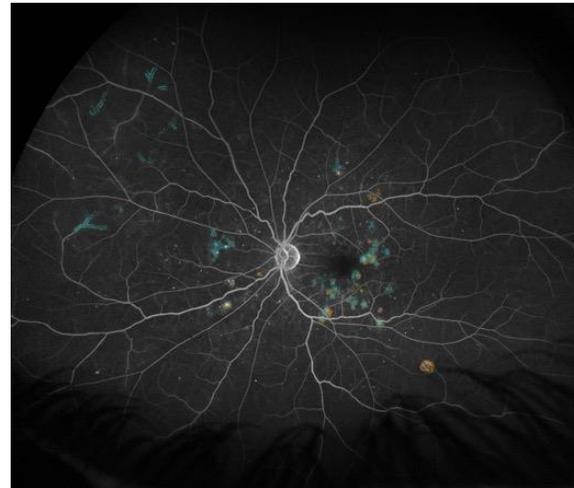


Case Example: OTX-TKI Patient

BASELINE



END OF STUDY



Quantitative Analysis of Retinal Vascular Leakage in HELIOS Phase 1 Trial

Key Takeaways

A single OTX-TKI injection may provide **sustained reductions in retinal leakage** across the peripheral retina, posterior pole, and total retinal area for up to 12 months.

These results, together with previously reported **DRSS improvement** and the **absence of vision threatening complications** at Week 48, support the potential of OTX-TKI as a **long-acting treatment option for diabetic retinopathy**, warranting further clinical investigation.

Study limitations include small sample size and assuming observed effect is comparable to true effect.

Thank You!