Volumetric Macular Fluid Analysis of the Impact of a Single Axitinib Intravitreal Implant (OTX-TKI) from the HELIOS Clinical Trial for Diabetic Retinopathy

Justis P. Ehlers, MD

The Norman C. and Donna L. Harbert Endowed Chair for Ophthalmic Research
Vice Chair for Continuous Improvement
Director, The Tony and Leona Campane Center for Excellence in Image-Guided Surgery and Advanced Imaging Research
Cole Eye Institute at Cleveland Clinic, Cleveland, OH

Angiogenesis, Exudation, and Degeneration | February 8, 2025 | Virtual

Disclosures

PRESENTER DISCLOSURES

Grant Support: Novartis, Zeiss, Alcon, Abbvie, Allergan, Adverum, Oxurion, Perceive Biotherapeutics, Roche, Stealth, Iveric Bio, Ocular Therapeutix, and Regeneron

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

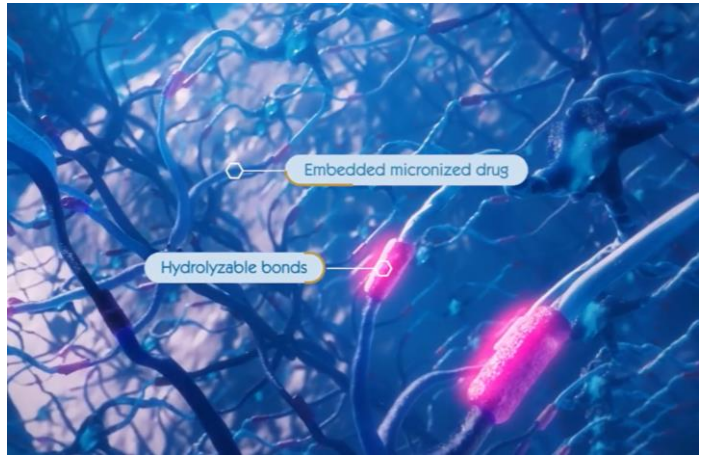
---

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

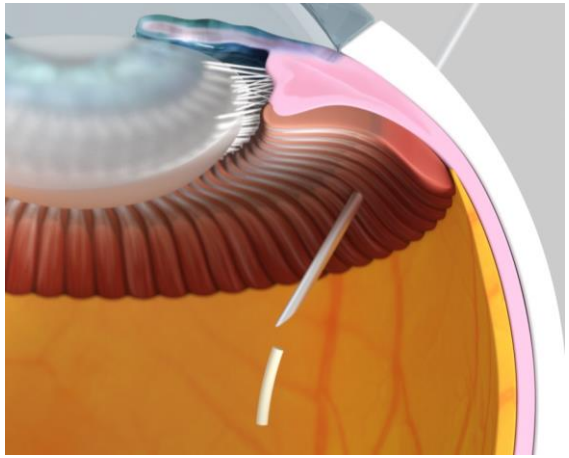
- Proprietary bioresorbable polymer matrix is a hydrogel-based, versatile, biocompatible platform for localized sustained drug delivery

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 vorolanib[1-3]
- Highly selective for all VEGF receptors[4-6] with no TIE2 inhibition at physiologic tissue concentrations[1]



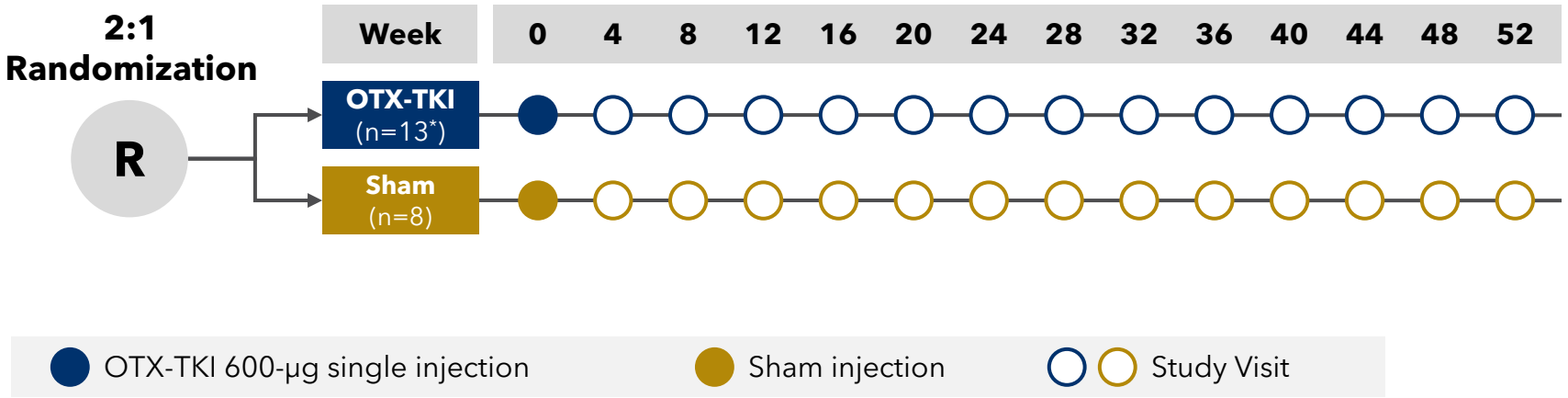
OTX-TKI

Single Intravitreal Bioresorbable Hydrogel Injection

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

HELIOS Phase 1 Study of OTX-TKI in NPDR

HELIOS



Multicenter, double-masked, randomized, parallel group study of OTX-TKI in patients with **moderately severe to severe NPDR without CI-DME** (as assessed by the investigator)

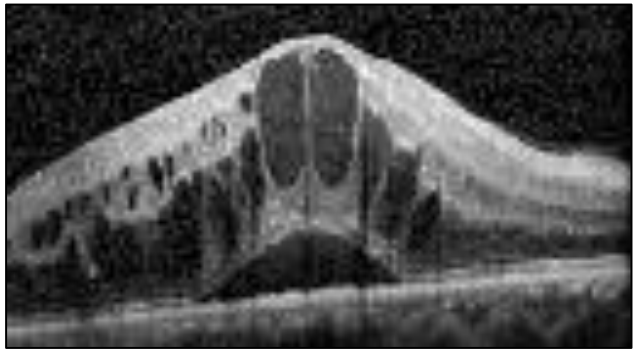
STUDY OUTCOMES

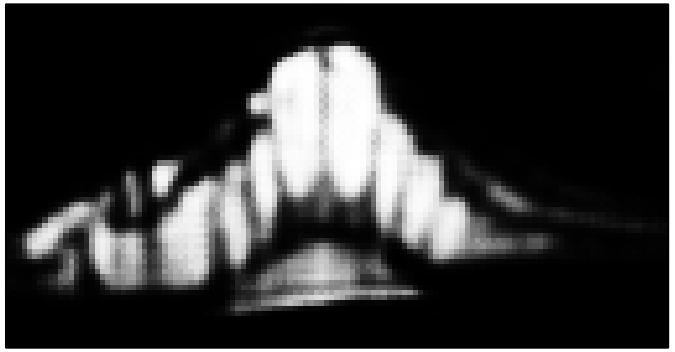
PRIMARY: Safety and tolerability of OTX-TKI

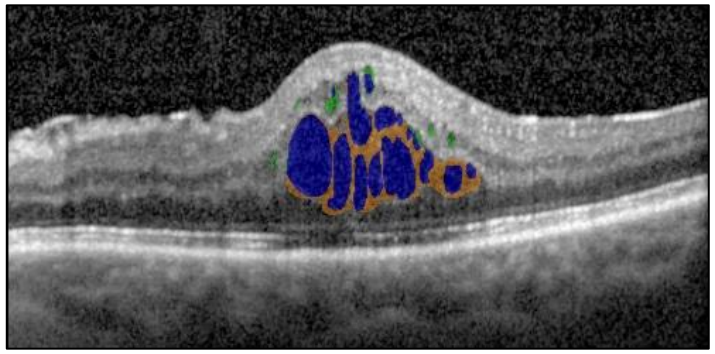
SECONDARY: DRSS changes, rescue therapy, BCVA, and CSFT changes

Multi-Layer and Fluid Feature OCT Analysis

- Post-hoc masked assessment for advanced OCT feature analysis
- Multi-model machine learning enhanced segmentation and feature extraction performed with certified reader validation across macular cube.
- Analysis Features Assessed:
  - Intraretinal fluid
  - Subretinal fluid
  - Retinal thickness (i.e., ILM-RPE)

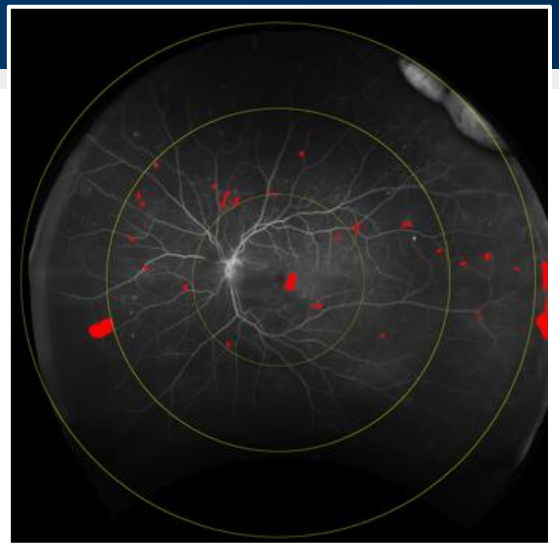


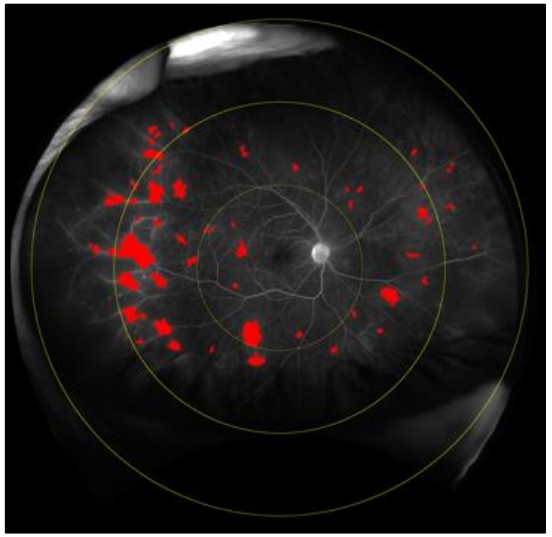




UWFA Quantitative Leakage Analysis

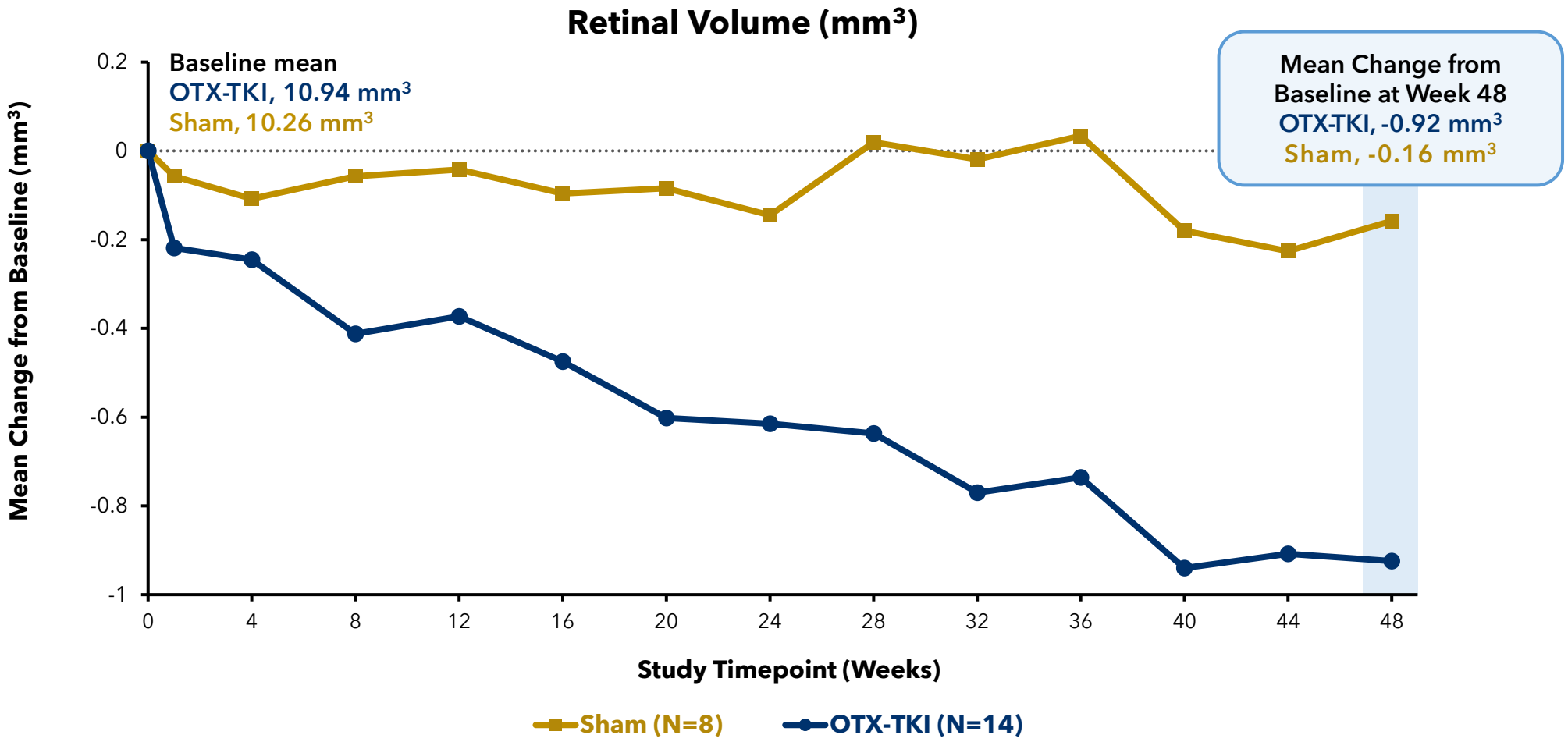
- Masked longitudinal assessment of quantitative leakage on UWFA images was conducted using a machine-learning augmented feature extraction platform.
- Leakage index was calculated as the proportion of retinal leakage (ie, hyperfluorescence) within the analyzable retina area
- Leakage segmentation validation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



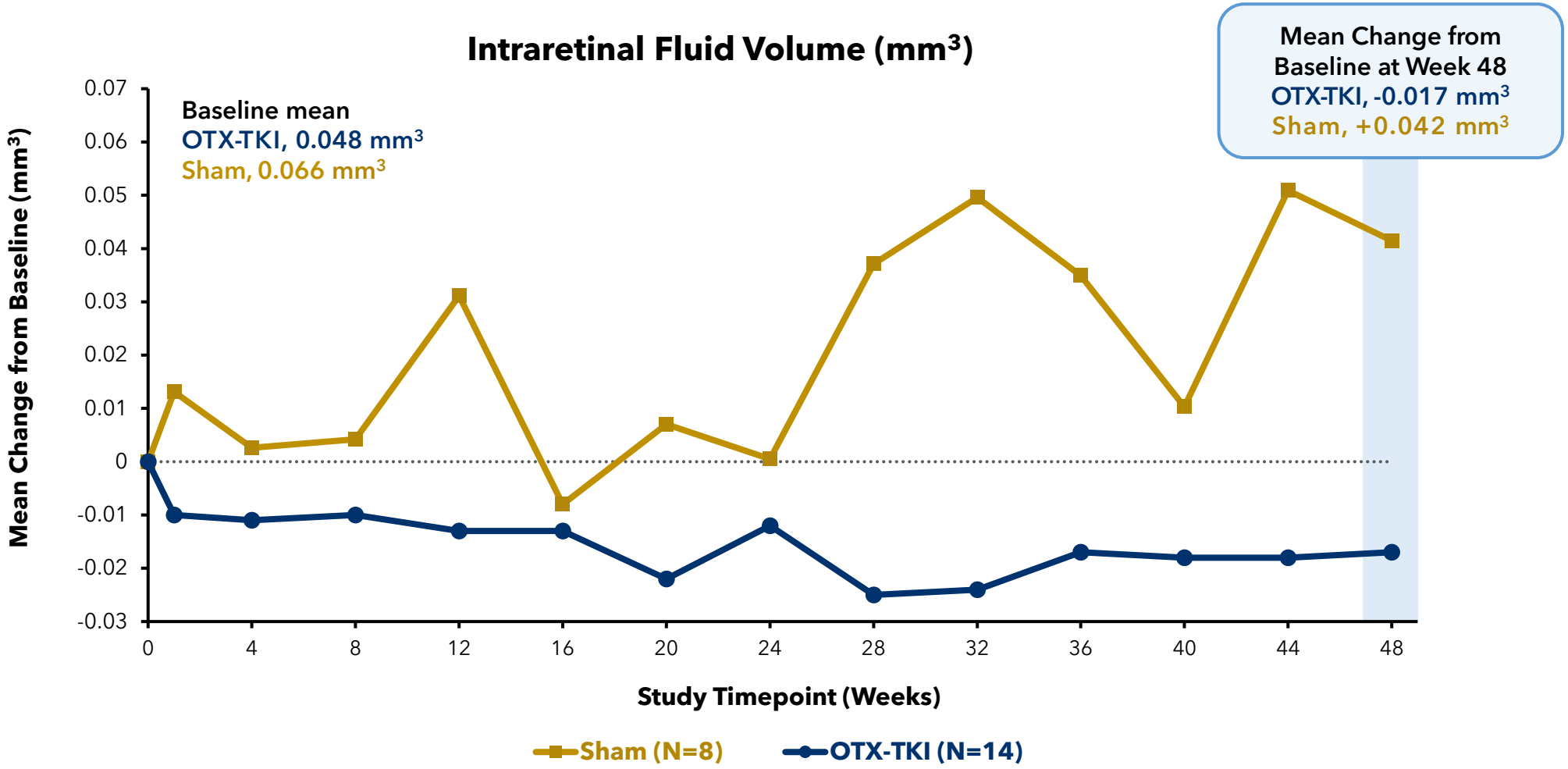


OCT ANALYSIS RESULTS

OTX-TKI Patients Consistently Had Greater Reductions from Baseline in Retinal Volume Compared to Sham

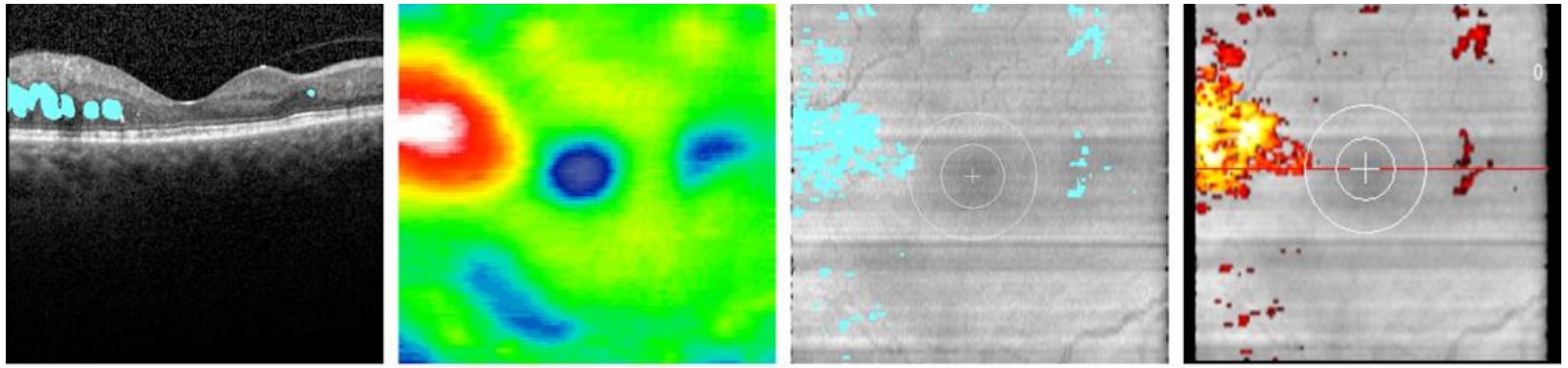


Sustained Control of Intraretinal Fluid in OTX-TKI Patients Over 48 Weeks



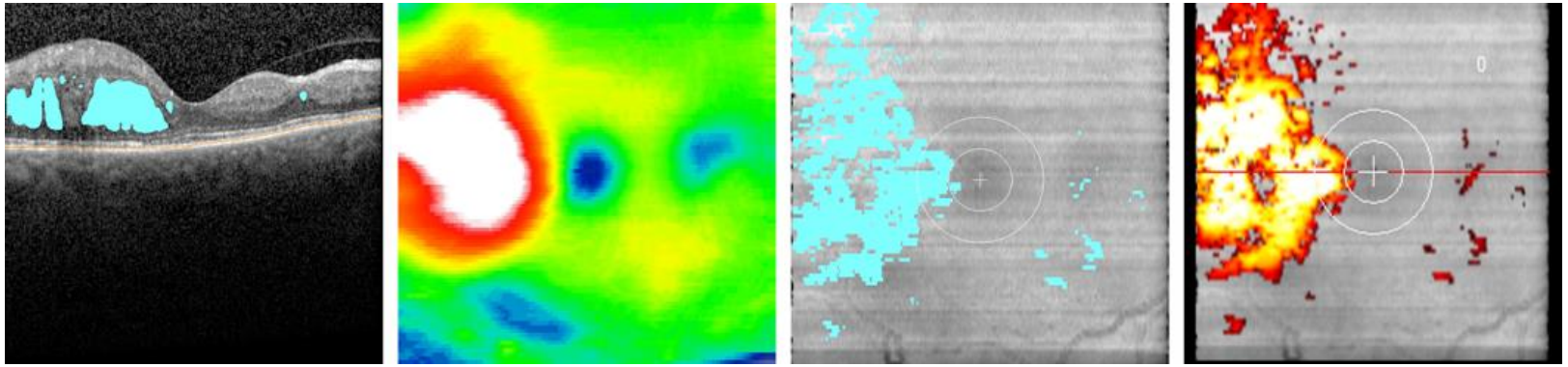
Case Example: Sham Patient

BASELINE



Foveal B-Scan | ILM/RPE Thickness Map | IRF Map | Fluid Thickness Map

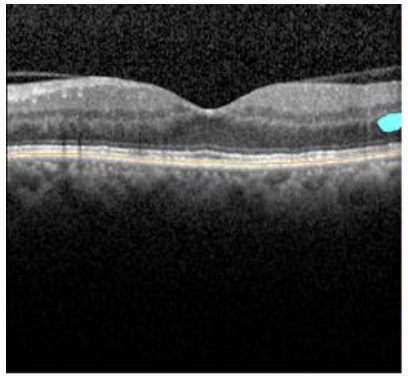
WEEK 48



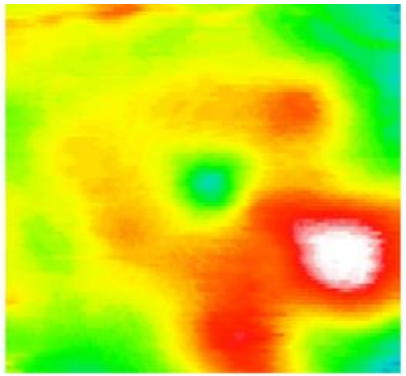
Foveal B-Scan | ILM/RPE Thickness Map | IRF Map | Fluid Thickness Map

Case Example: OTX-TKI Patient

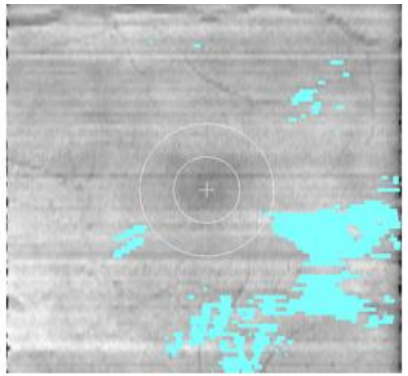
BASELINE



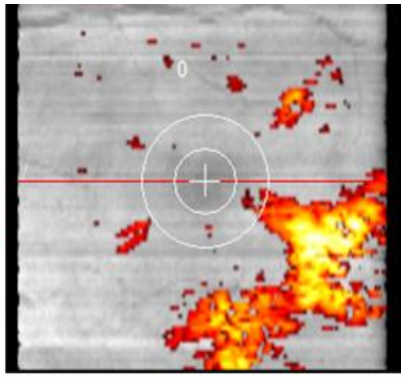
Foveal B-Scan



ILM/RPE Thickness Map

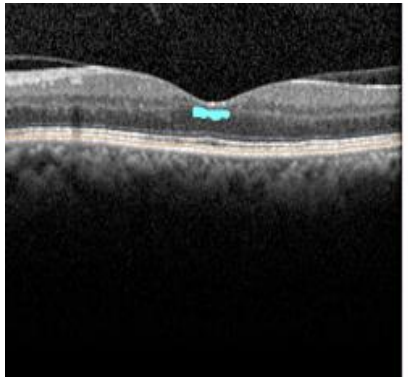


IRF Map

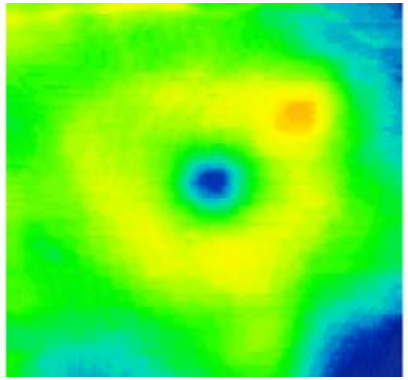


Fluid Thickness Map

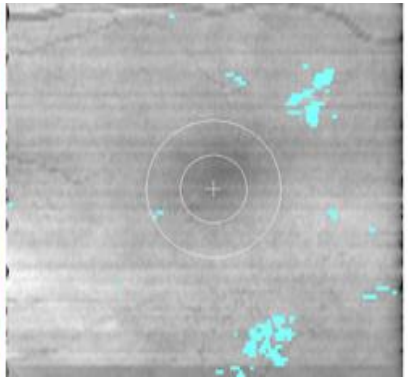
WEEK 48



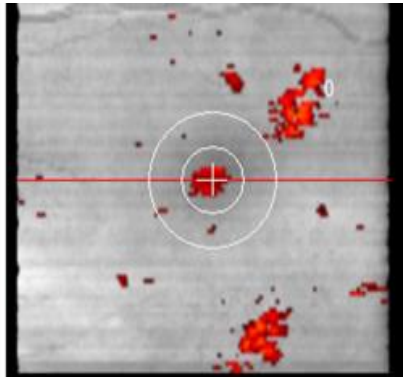
Foveal B-Scan



ILM/RPE Thickness Map



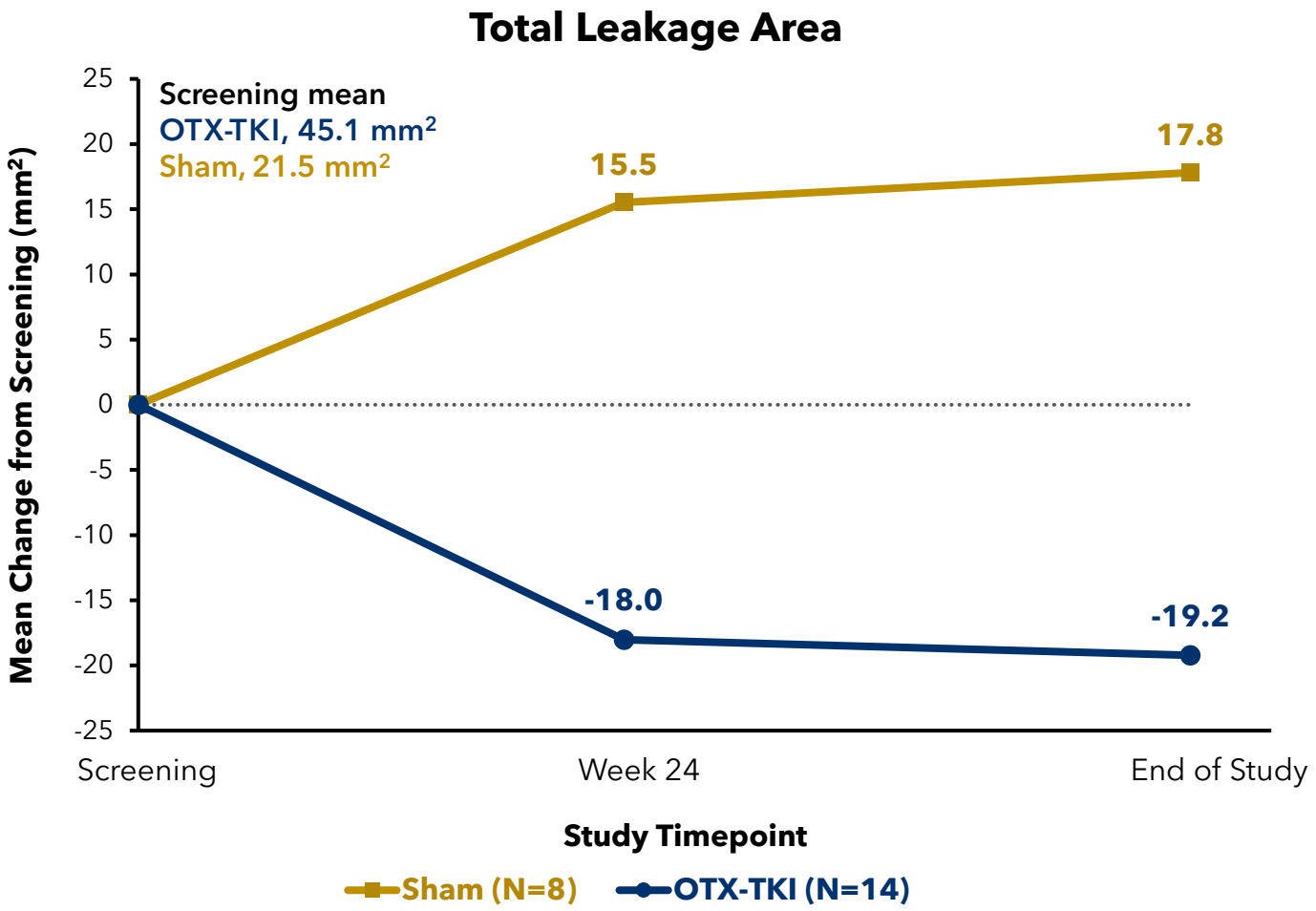
IRF Map

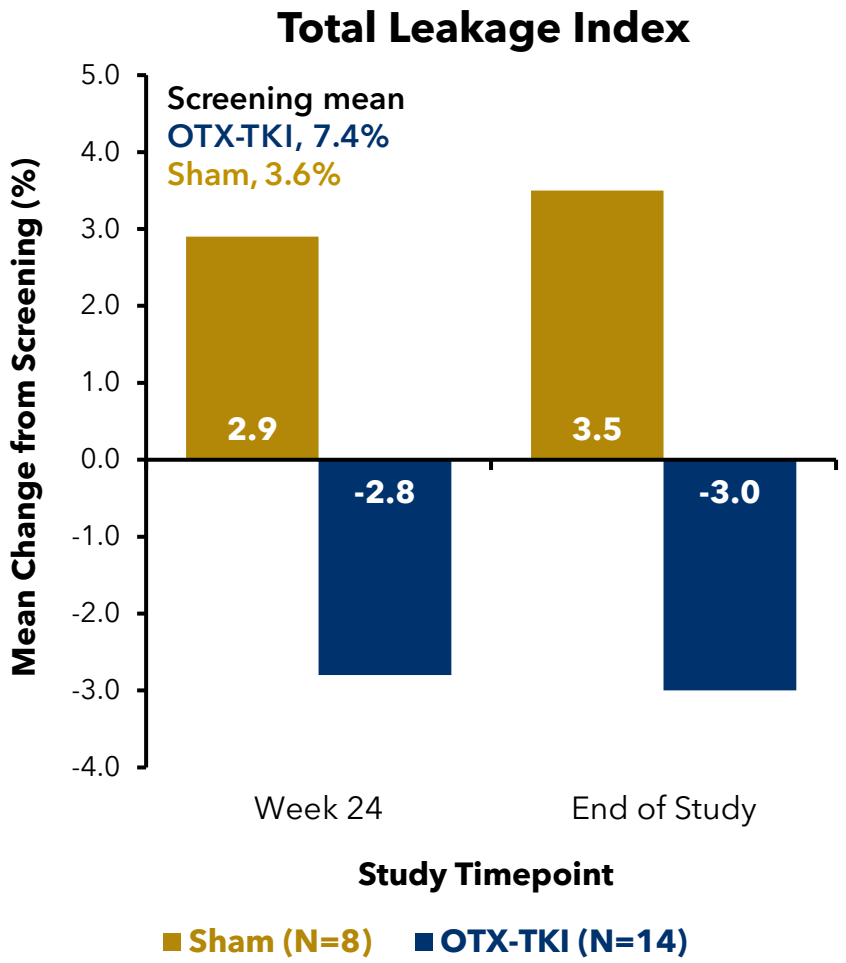


Fluid Thickness Map

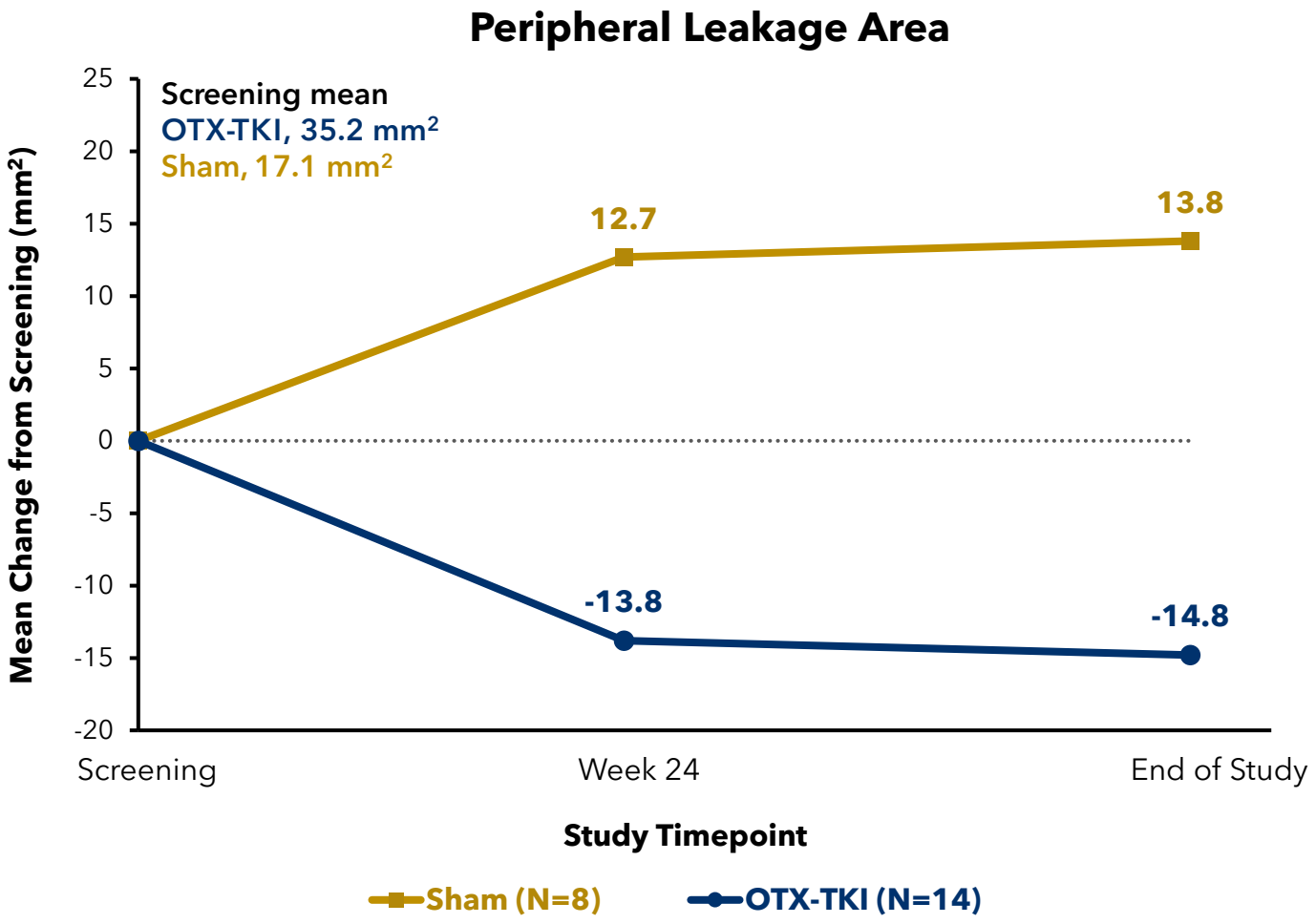
UWFA ANALYSIS RESULTS

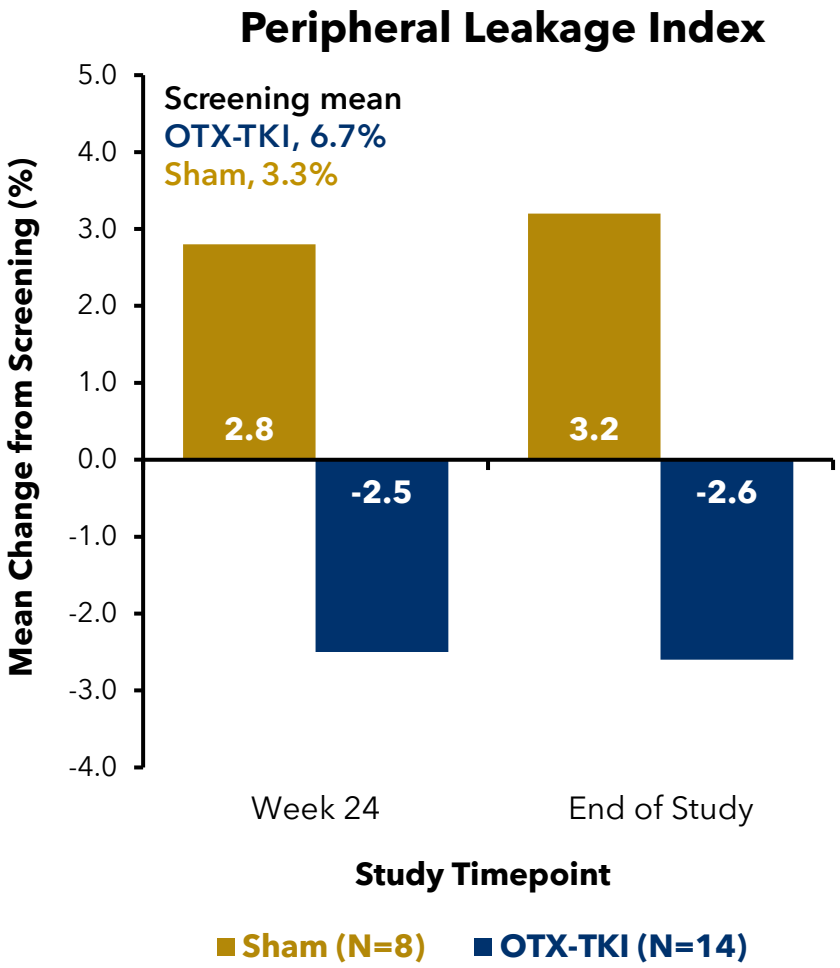
Durable Reduction in Total Retinal Vascular Leakage Across One Year Observed with OTX-TKI Compared to Sham



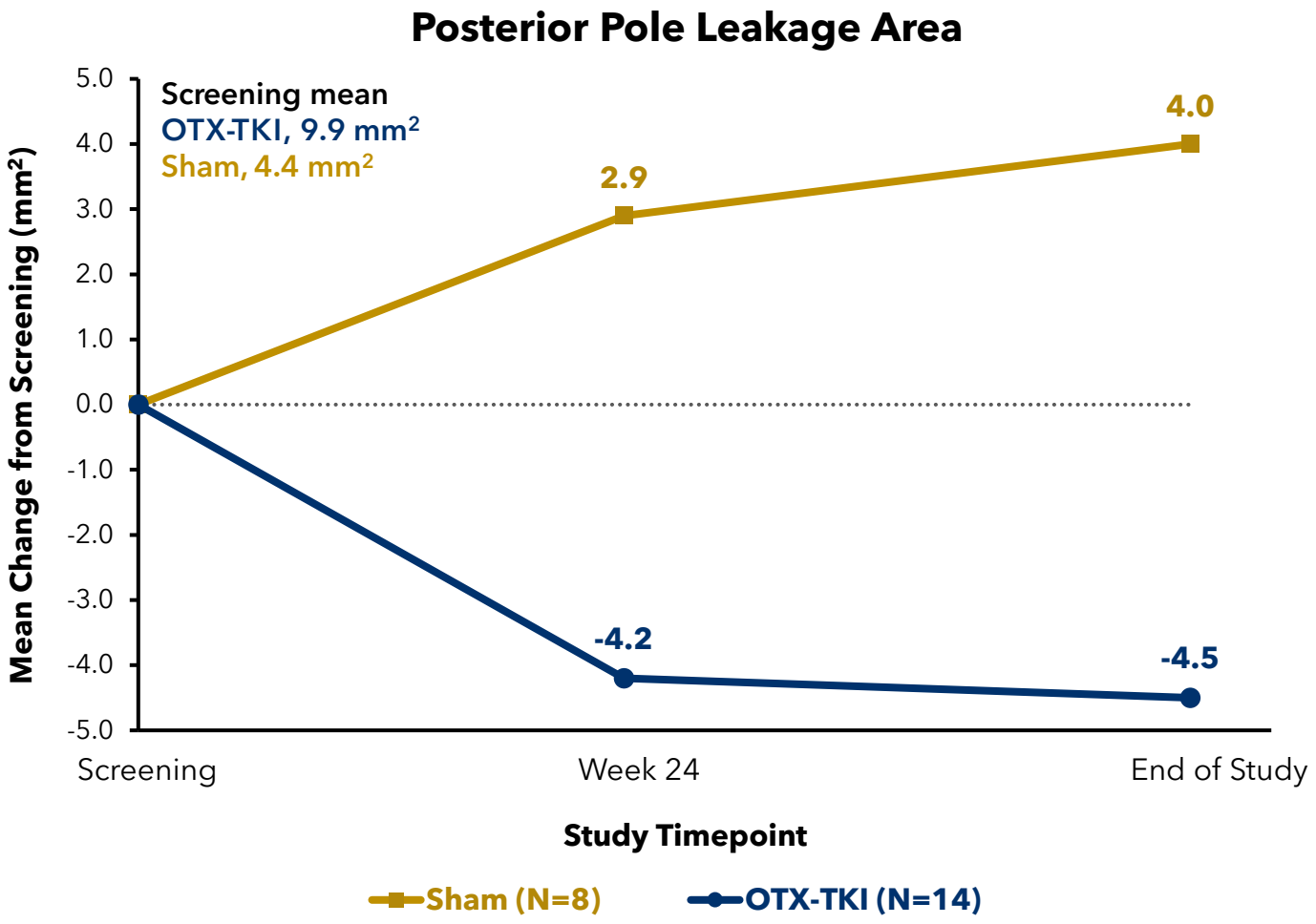


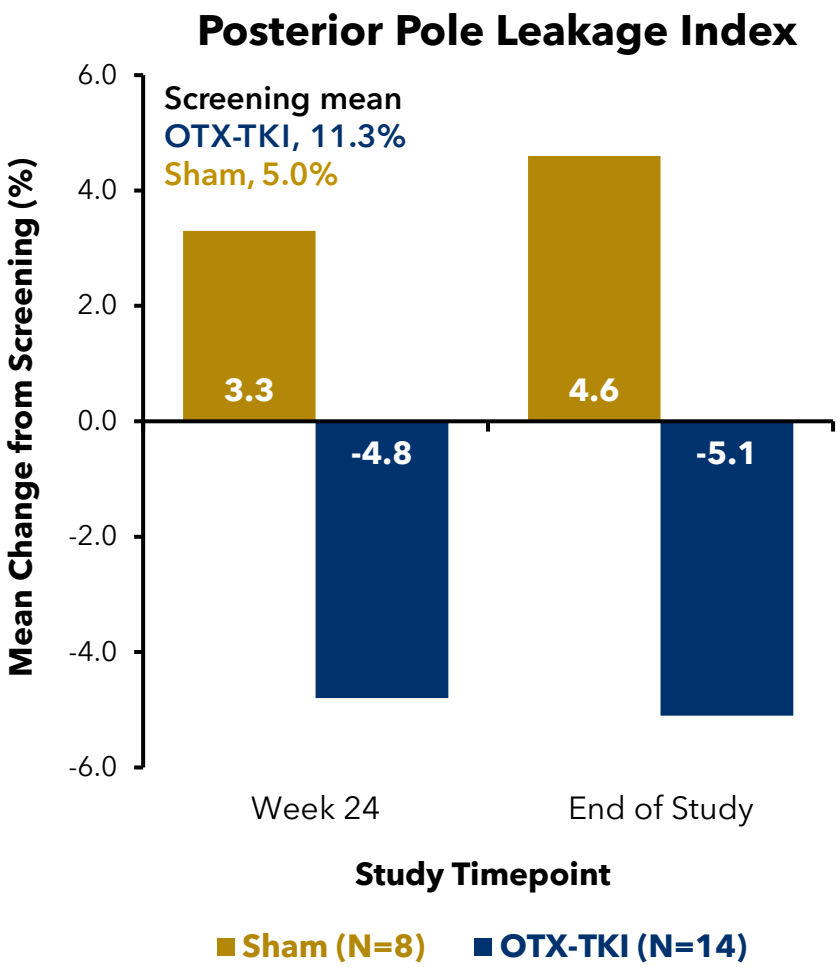
Peripheral Leakage Parameters Improved in OTX-TKI Eyes, While Worsening Was Observed in Sham Eyes





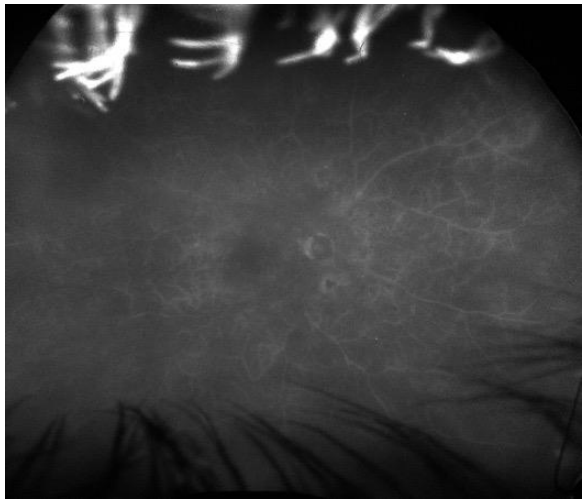
OTX-TKI Eyes Show Sustained Reduction in Leakage Parameters Across Posterior Pole

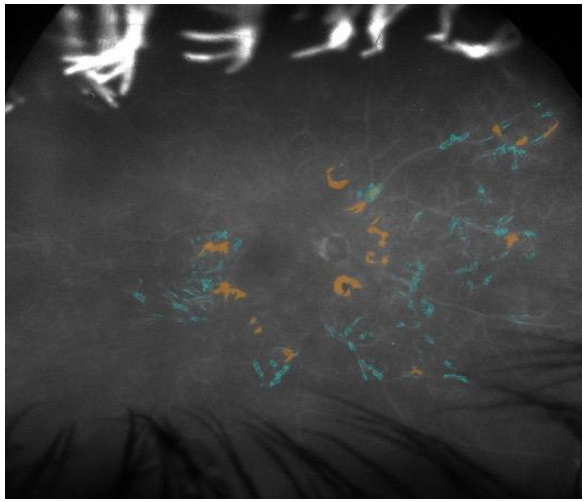




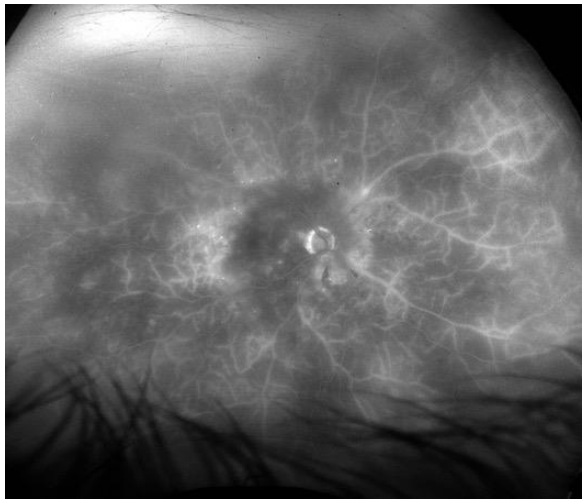
Case Example: Sham Patient

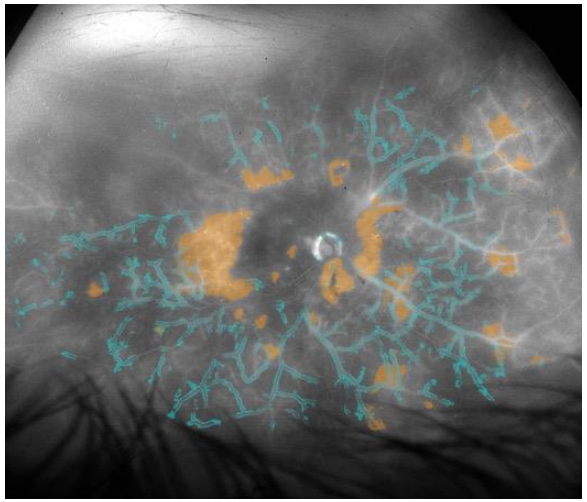
BASELINE





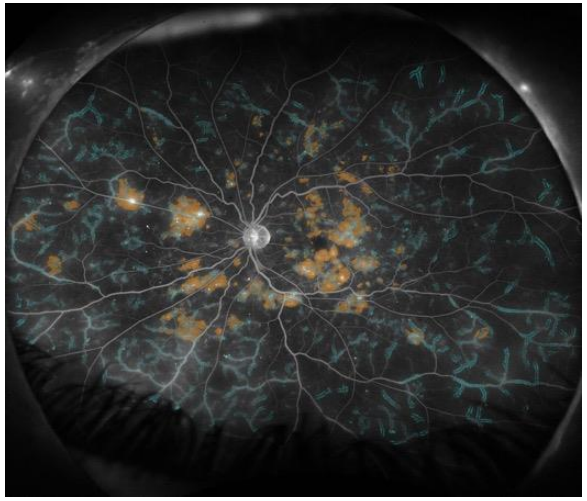
END OF STUDY



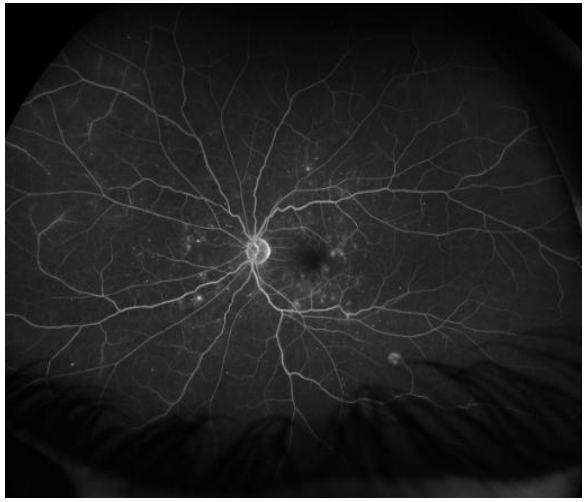


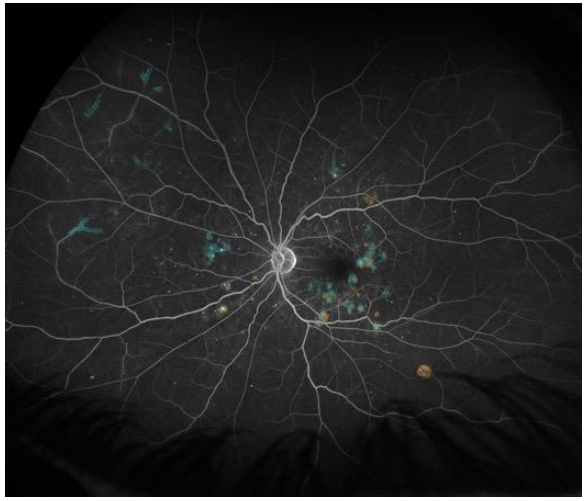
Case Example: OTX-TKI Patient

BASELINE



END OF STUDY





Quantitative Analysis of Macular Fluid Volumes and Retinal Vascular Leakage in HELIOS Phase 1 Trial Key Takeaways

Consistent improvement in fluid metrics was observed in OTX-TKI–treated patients compared to sham

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 support the potential of OTX-TKI as a long-acting treatment option for diabetic retinopathy, warranting further clinical investigation

Acknowledgements

The Tony and Leona Campane Image-Guided Surgery and Advanced Imaging Lab

- Sunil K. Srivastava, MD
- Ming Hu, PhD
- Jon Whitney, PhD
- Michelle Bonnay
- Neal Shah, MD
- Devesh Kumar, MD
- Masaharu Mizuno, MD PhD
- Scott Perkins
- Jasmine Scafuro
- Julie Baraona, PA-C
- Jamie L. Reese, BSN
- Karen Matar, MD
- Asmita Indurkar, MD
- Melanie Jennings
- John Mamone
- Amy Tang
- Julia Beilis
- Richa Vallurupalli
- Elise Milliner
- Katherine Talcott, MD
- Hasan Cetin, MD
- Reem Amine, MD
- Jordan Budrevich
- Lyndsey DellaVecchia
- Erin Flannigan
- Penina Schlesinger
- Barret Schmidt
- Karissa Zarbock