Sustained-Release Axitinib Hydrogel (OTX-TKI) for Wet AMD: US Phase 1 Study Results

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Disclosures and Disclaimers

PRESENTER DISCLOSURES (PATRICIO SCHLOTTMANN, MD)

No financial disclosures to declare.

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

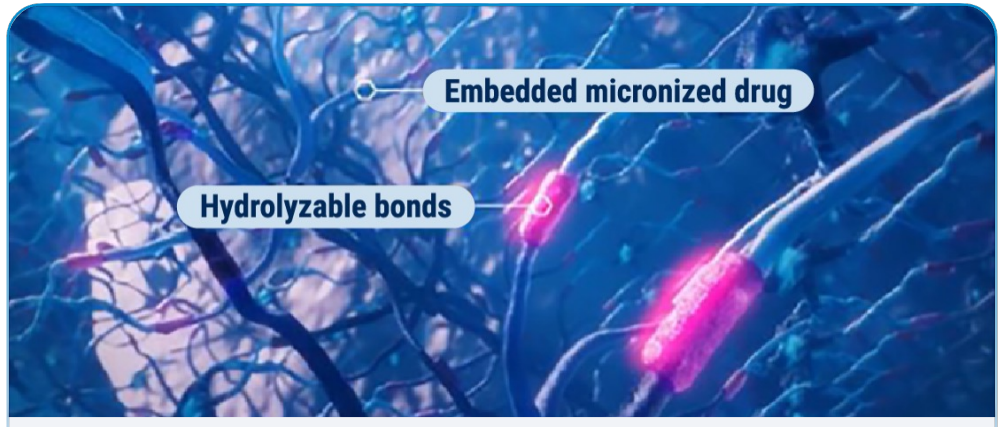
AXITINIB

Multi-target Tyrosine Kinase Inhibitor (TKI)

Highly selective pan VEGF inhibitor[1]
Most potent TKI[2]

ELUTYX™ TECHNOLOGY

Bioresorbable, Sustained Drug Delivery



Proprietary hydrogel
Versatile, biocompatible, tunable platform[3]

OTX-TKI

Single injection, single hydrogel[3]

Continuous and consistent delivery up to 12 months[3]

Complete and predictable bioresorption[3]

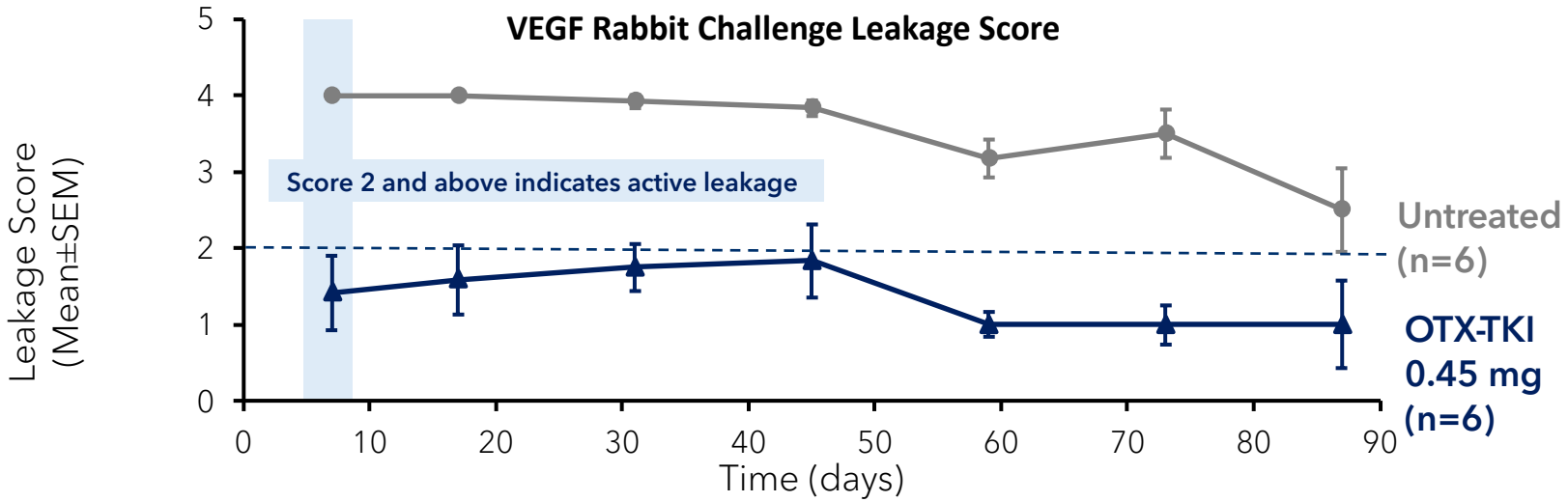
Abbreviations: IC (inhibitory concentration); KDR (kinase domain receptor); TIE2 (Tyrosine kinase with immunoglobulin-like and EGF-like domains-2); TKI (Tyrosine kinase inhibitor); VEGF (Vascular endothelial growth factor [receptor]).

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 Unpublished data; Data on File. 2.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. 7. Blizzard CD, et al. US Patent: Ocular implant containing a tyrosine kinase inhibitor. Published online September 13, 2022. Accessed September 26, 2022.

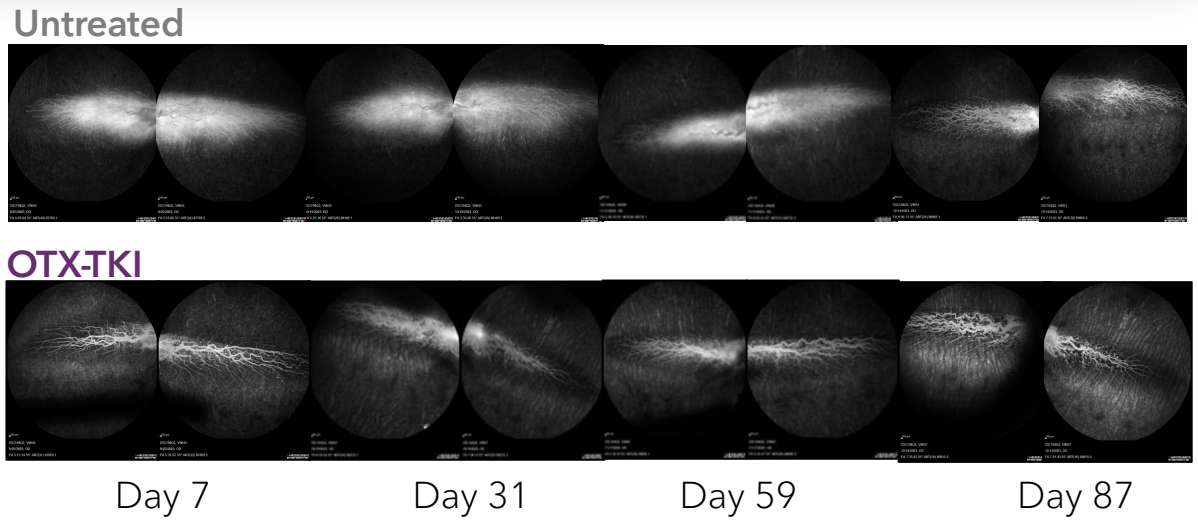
Pre-clinical VEGF-Challenged Rabbits Sustain Rapid Reduction in Vascular Leakage Following OTX-TKI Injection

OTX-TKI demonstrated:

- Early onset **leakage reduction at Day 7** post-VEGF challenge
- Maintained low leakage scores throughout the study period



Score	Scoring Descriptor
0	Major vessels straight, some tortuosity of smaller vessels, no vessel dilation
1	Increased tortuosity of major vessels and/or some vessel dilation
2	Leakage between major vessels, significant vessel dilation
3	Leakage between major and minor vessels, minor vessels still visible
4	Leakage between major and minor vessels, minor vessels poorly/not visible



VEGF (Vascular endothelial growth factor).

Blizzard, Chuck, Patel, Chintan, Patil, Madhoosudan, Kahn, Erica, Iacona, Joe, Domingues, Daniel, Whalen, Alyssa, Sherman, Olivia, Haswani, Dinesh, Jarrett, Peter, Gurses Ozden, Rabia. Pharmacodynamic Efficacy of Optimized Intravitreal Axitinib Implant (OTX-TKI) in a VEGF Challenge Rabbit Model. Paper presented at: Association for Research in Vision and Ophthalmology; May 9, 2024; Seattle, USA.

Phase 1 nAMD Trials Provides Evidence of Biological Activity for OTX-TKI in Two Patient Populations

Australia
Phase 1 Trial

Dose Escalation (Safety): Does OTX-TKI have biological activity?

Open-Label, Dose Escalation Trial[1]

- To evaluate the safety and biological activity of OTX-TKI in **treatment naïve or previously treated active** wet AMD patients
- Results provided evidence of potential as a durable **sustained-release product with biological activity in subjects with pre-existing fluid**

U.S.
Phase 1 Trial

Biological Activity: How long does the biological activity signal of OTX-TKI last?

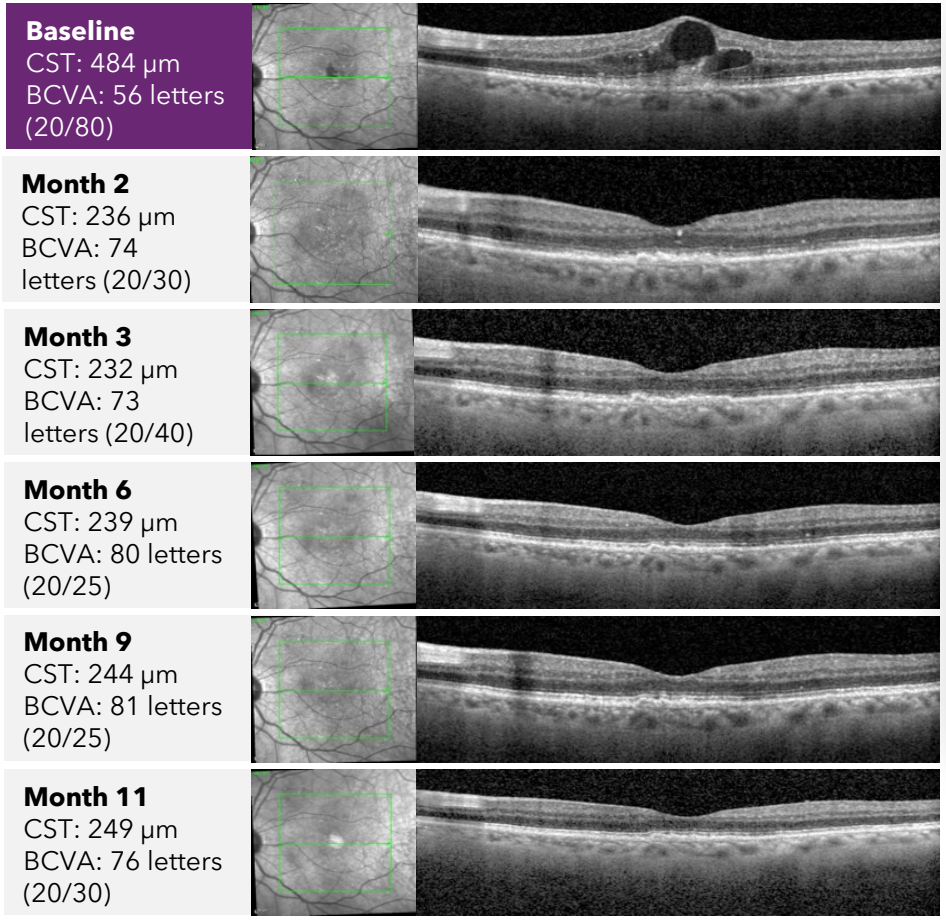
Randomized, Masked, Controlled Trial[2]

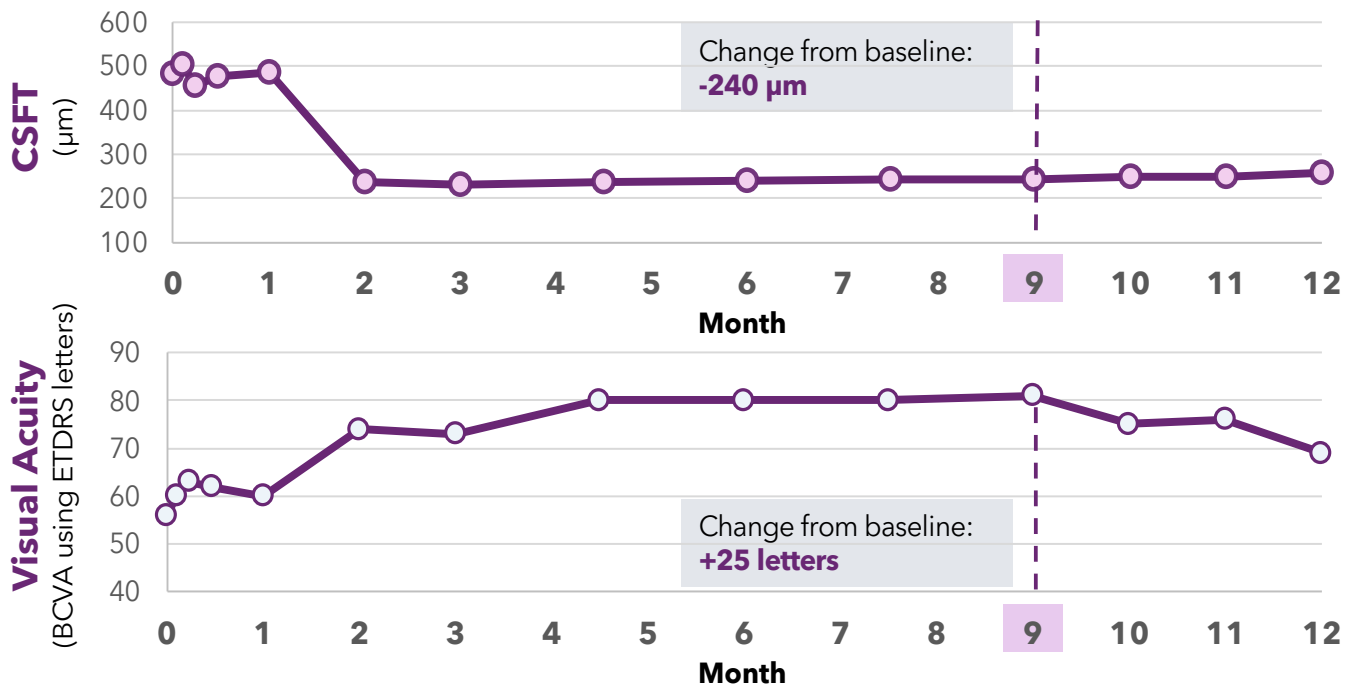
- To evaluate the safety and biological activity of OTX-TKI in **previously treated controlled** wet AMD patients compared to aflibercept Q8W
- 12-month results provided evidence of potential as a durable **sustained-release maintenance therapy for 6-12 months in subjects with controlled retinal fluid**

1. Kaiser PK, et al. Presented at Eyecelerator at American Academy of Ophthalmology Meeting, Retina Showcase, Sep 29, 2022; 2. Moshfeghi A et al. Presented at American Academy of Ophthalmology Meeting, Sept 2022
nAMD (neovascular age-related macular degeneration)

OTX-TKI Case Study: Sustained Response Observed in Treatment-Naïve Subject

CSFT and Vision Improved Following Treatment with 600 µg OTX-TKI





The subject only received OTX-TKI and remained supplemental injection-free

BCVA (Best corrected visual acuity); CST (Central subfield thickness); ETDRS (Early Treatment Diabetic Retinopathy Study).

Phase 1 OTX-TKI US-Based nAMD Clinical Trial Design

Multicenter, Randomized, Double-masked Trial

Screening

Key Inclusion Criteria

- Sub foveal neovascularization secondary to AMD
- **Controlled fluid**
- **Previously treated with anti-VEGF injections**

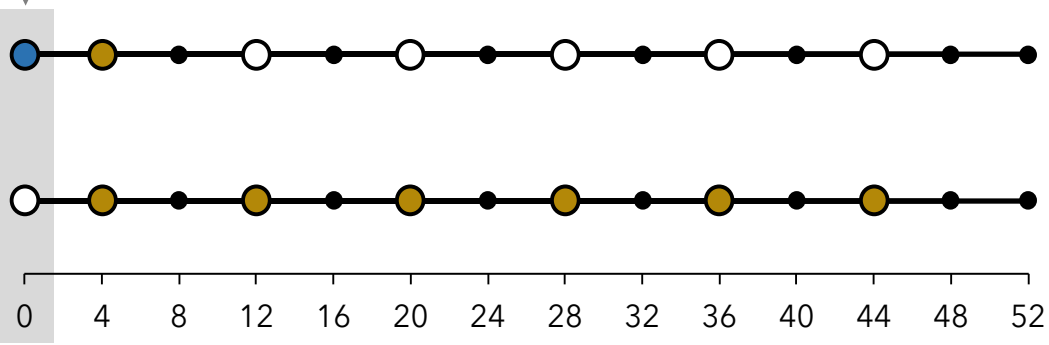
R

Randomization 3:1 (OTX-TKI : Aflibercept)

Baseline

OTX-TKI Arm (n=15)

Aflibercept Arm (n=5)



Rescue Anti-VEGF Injection Criteria:

- Loss of ≥10 letters from best previous BCVA with current BCVA worse than baseline, or
- Evidence of ≥75µm CSFT increase from previous best value and ≥5 letters loss from best previous BCVA, or
- New macular hemorrhage

AAO=American Academy of Ophthalmology; AMD=age-related macular degeneration; BCVA=best corrected visual acuity; BL=baseline; CSFT=central subfield thickness; AMD=age-related macular degeneration; VEGF=vascular endothelial growth factor

Reference: Khanani AM, et al. 12-Month Update on Randomized, Controlled, Trial of OTX-TKI (Axitinib Intravitreal Implant) for the Treatment of Wet AMD. Presented at the Clinical Trials at the Summit. June 10, 2023. Park City, UT.

Phase 1 US: Safety Data

No reports of drug-related ocular or systemic SAEs in either arm

One event of acute endophthalmitis in the OTX-TKI arm that occurred following mandated aflibercept injection at Month 1

- Reported as moderate
- Injection procedure related, unrelated to study drug
- Resolved after IVT antibiotic injection, with vision returning to baseline

All events were mild except:

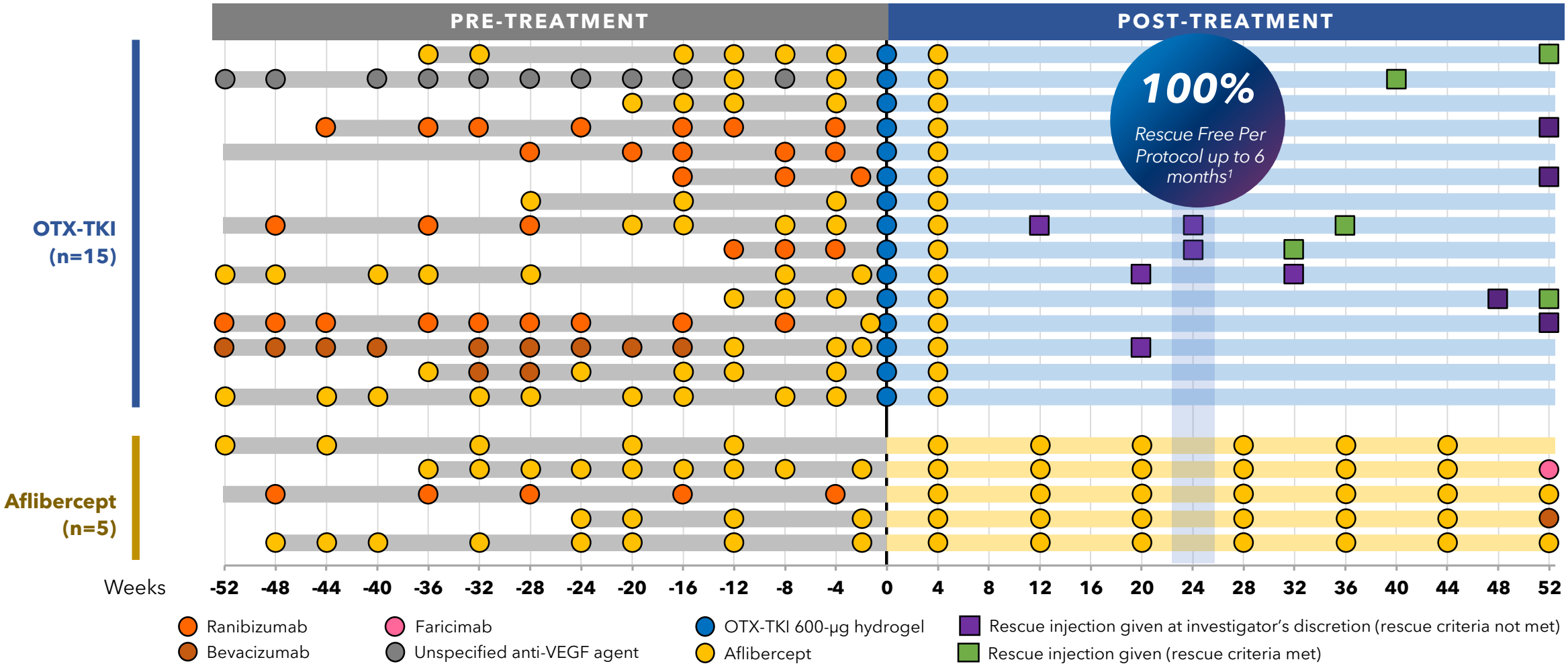
- Acute endophthalmitis SAE (moderate and resolved) and worsening of cataract (moderate) in OTX-TKI arm
- Elevated IOP in aflibercept arm (moderate and resolved)

	OTX-TKI N=16	AFLIBERCEPT N=5
Patients With AEs in the Study Eye, n (%)		
Elevated IOP	2 (12.5)	1 (20.0)[b]
Retinal detachment	0	0
Retinal vasculitis	0	0
Implant migration into the anterior chamber	0	N/A
Acute endophthalmitis	1 (6.25)[a]	0
Patients With Ocular AEs in the Study Eye Reported by Severity, n (%)		
Ocular AEs	16 (100.0)	3 (60.0)
Mild	14 (87.5)	2 (40.0)
Moderate	2 (12.5)[a]	1 (20.0)[b]
Severe	0	0
SAEs	1 (6.25)[a]	0

[a]Moderate and serious ocular AE in OTX-TKI arm was acute endophthalmitis 6 days after mandated aflibercept injection at Month 1.
[b]Moderate AE in aflibercept arm was elevated IOP.

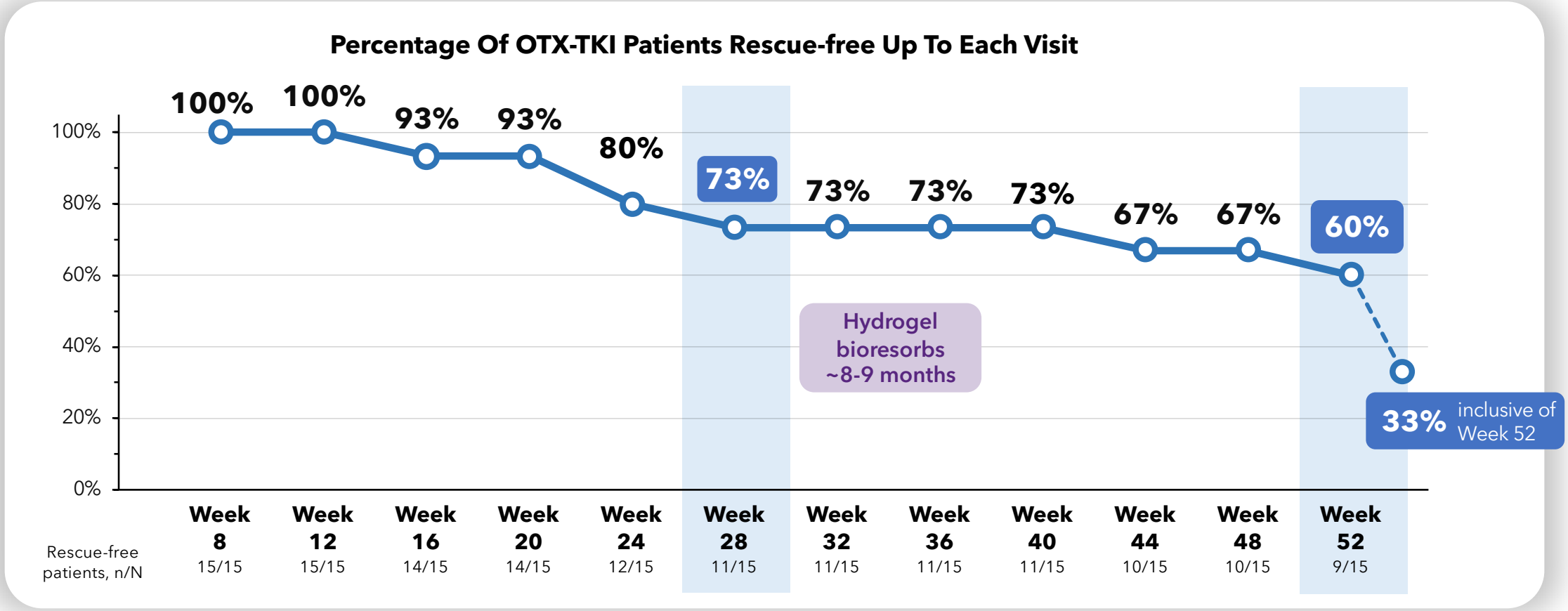
Data cut off April 14, 2023.
AE (Adverse event); IOP (Intraocular pressure); IVT (Intravitreal); SAE (Serious adverse event).

US Phase 1: 89% Reduction in Anti-VEGF Treatment Burden at Week 52 with OTX-TKI Treatment



Data cut off April 14, 2023; per protocol analysis. Reduction in treatment burden calculation includes all rescue injections. Sham injection was given at Week 0 in the aflibercept arm and at Weeks 12, 20, 28, 36, and 44 in the OTX-TKI arm (not shown). At Week 52, patients in the aflibercept group were treated with wet AMD standard of care at the investigator's discretion. VEGF (Vascular endothelial growth factor).

US Phase 1: OTX-TKI Observed Extended Duration of Action

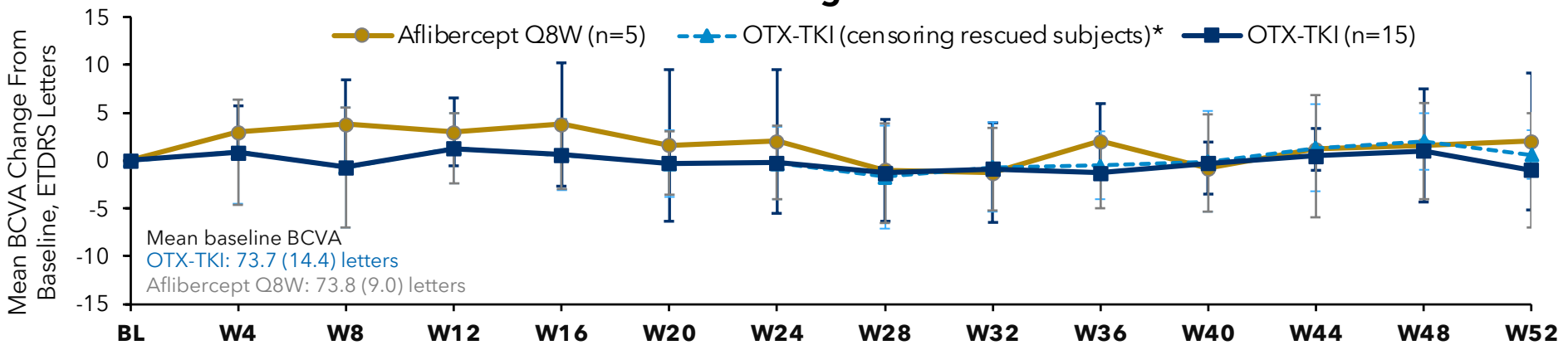


73% of OTX-TKI-treated patients were rescue-free up to 28 weeks, 60% up to 52 weeks

Data cut off April 14, 2023. Rescue-free rate calculations: If patients received rescue anti-VEGF therapy at a study visit, those were reflected at the following study visit in the graph above. Percentages presented in the graph above represent rescue-free rates up to each study visit, except for the 33% at Week 52, which includes rescue injections given at the Week 52 study visit.
VEGF (Vascular endothelial growth factor).

US Phase 1: OTX-TKI BCVA, CSFT Results Similar to Aflibercept 2mg Q8W Arm

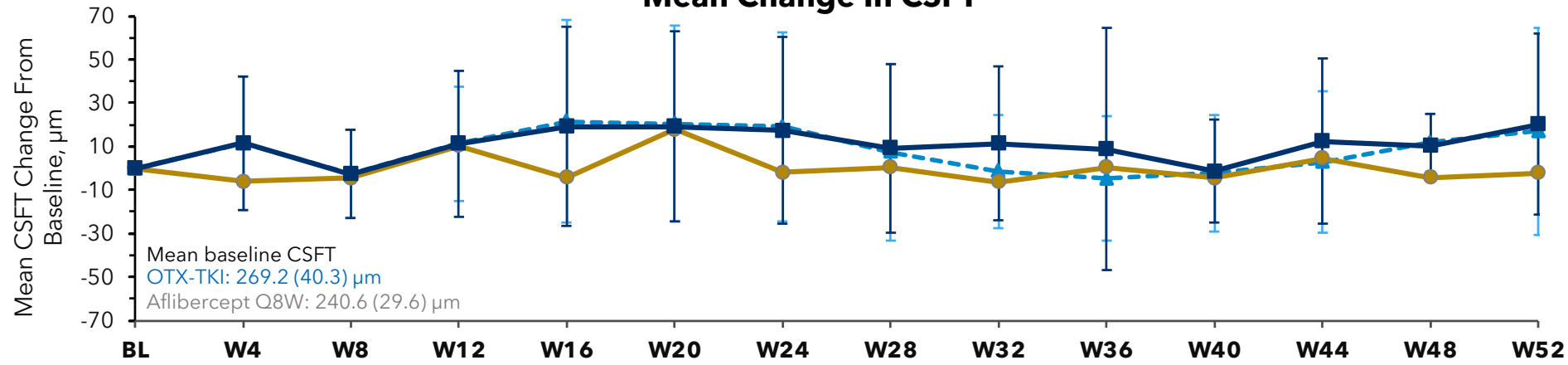
Mean Change In BCVA



Mean (SD) change in BCVA from baseline to Week 52:

- OTX-TKI: -1.0 (6.0) letters
- OTX-TKI: +0.6 (2.6) letters (censoring rescued subjects)
- Aflibercept Q8W: +2.0 (7.2) letters

Mean Change In CSFT



Mean (SD) change in CSFT from baseline to Week 52:

- OTX-TKI: +20.2 (41.6) µm
- OTX-TKI: +17.2 (47.6) µm (censoring rescued subjects)
- Aflibercept Q8W: -2.2 (8.5) µm

Data cut off April 14, 2023. n=14 in OTX-TKI arm at Weeks 8, 28, 40, and 48 due to missed visits.
*Sample size for OTX-TKI (censoring rescued patients): n=15 at baseline and Weeks 4 and 12; n=14 at Week 8 (missed visit) and Weeks 16 and 20; n=12 at Week 24 and n=11 at Weeks 28, 32, 36, and 40; n=10 at Week 44; n=9 at Weeks 48 and 52; BCVA (Best corrected visual acuity); BL (Baseline); CSFT (Central subfield thickness); ETDRS (Early Treatment Diabetic Retinopathy Study).

Retinal Fluid Fluctuations are a Predictor of Poor Long-Term Visual Outcomes

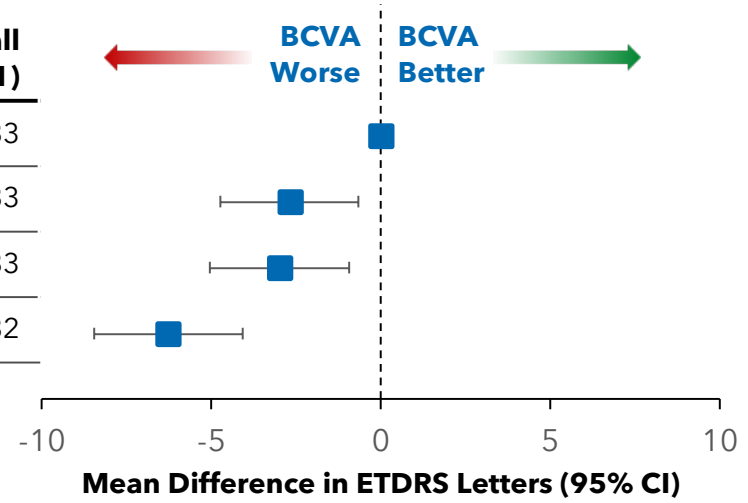
JAMA Ophthalmology | Original Investigation

Associations of Variation in Retinal Thickness With Visual Acuity and Anatomic Outcomes in Eyes With Neovascular Age-Related Macular Degeneration Lesions Treated With Anti-Vascular Endothelial Growth Factor Agents

Rebecca N. Evans, MSc; Barnaby C. Reeves, DPhil; Maureen G. Maguire, PhD; Daniel F. Martin, MD; Alyson Muldrew, PhD; Tunde Peto, MD, PhD; Chris Rogers, PhD; Usha Chakravarthy, MD, PhD

ASSOCIATION BETWEEN RETINAL THICKNESS FLUCTUATIONS AND VISION[1]

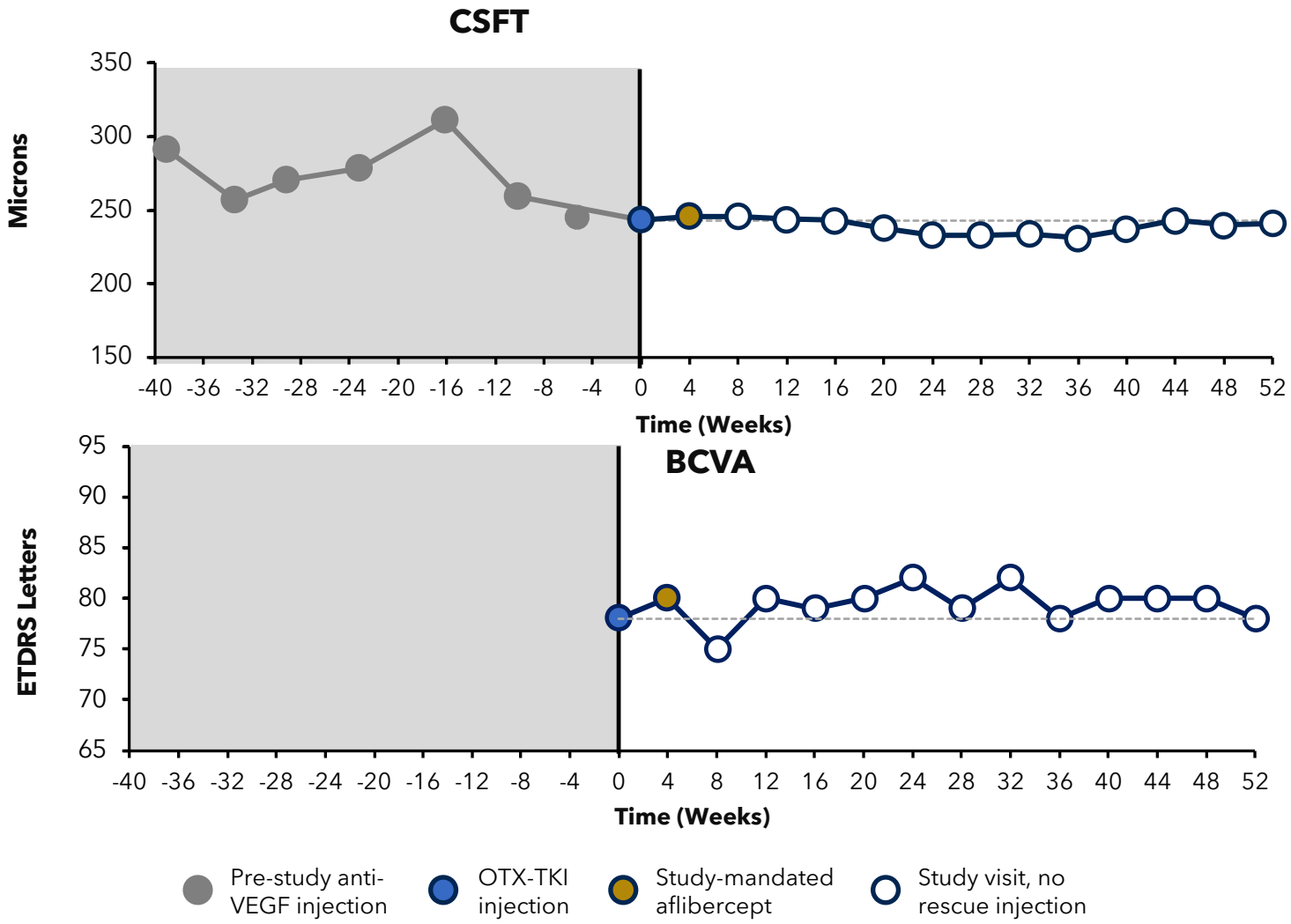
Foveal Center Point Thickness Standard Deviations	Overall (n = 1731)
Quartile 1 (least fluctuations) [reference]	n=433
Quartile 2	n=433
Quartile 3	n=433
Quartile 4 (most fluctuations)	n=432

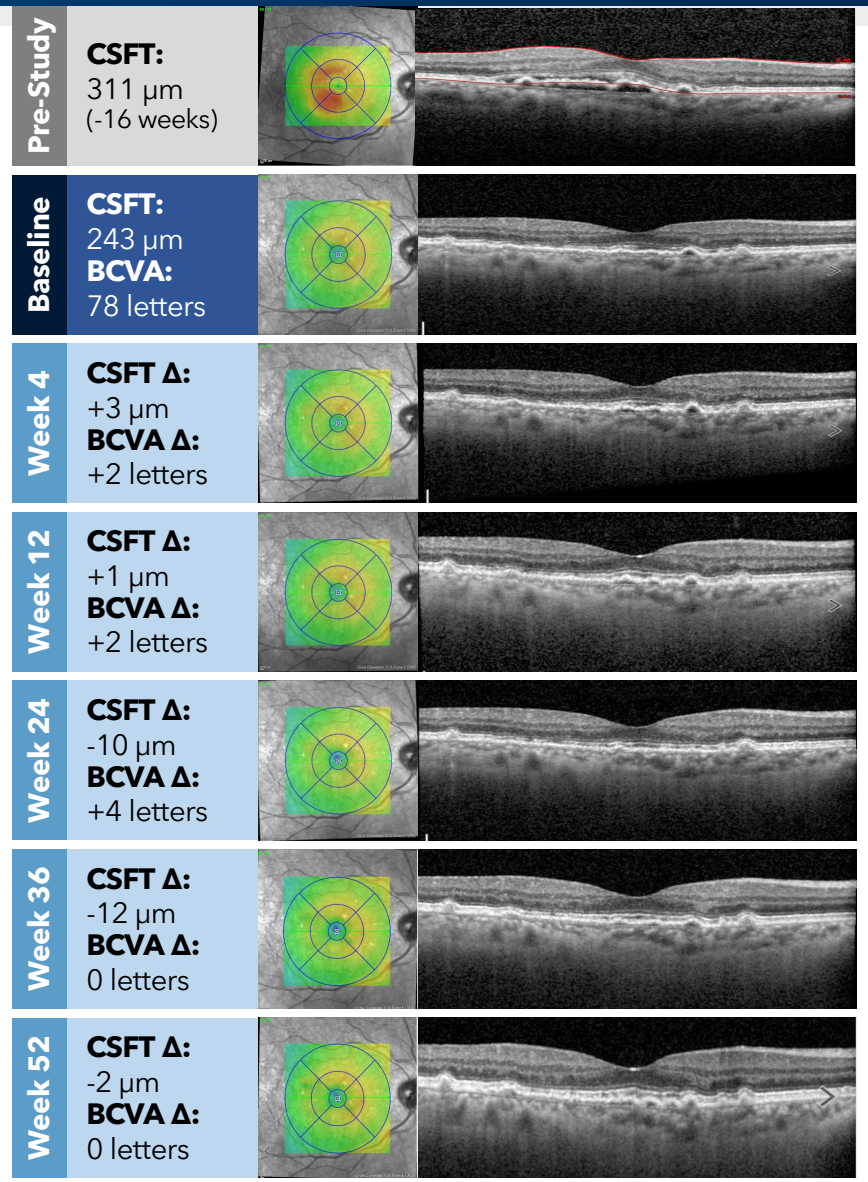


1. Evans RN, et al. JAMA Ophthalmol. 2020 Oct 1;138(10):1109. 2. Sheth V, et al. BMJ Open Ophthalmol. 2022;7(1):e000957. 3. Chen AX, et al. Ophthalmol Retina. 2020;4(12):1158-1169.

Case Example: OTX-TKI Reduces Fluctuation in Fluid and CSFT for 1 Year

65yo female with anti-VEGF Q4-8W prior to study and rescue-free through 1 year

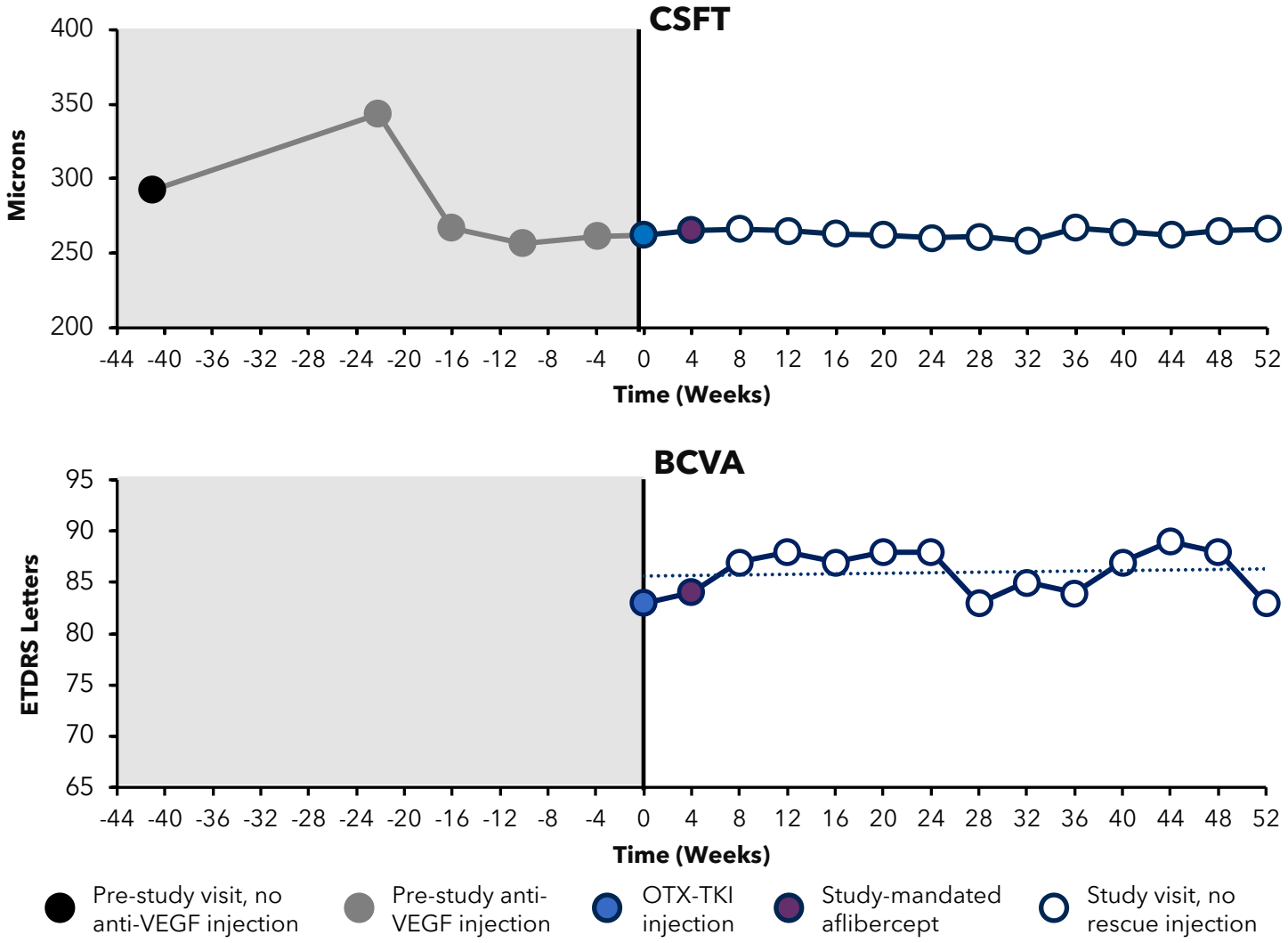


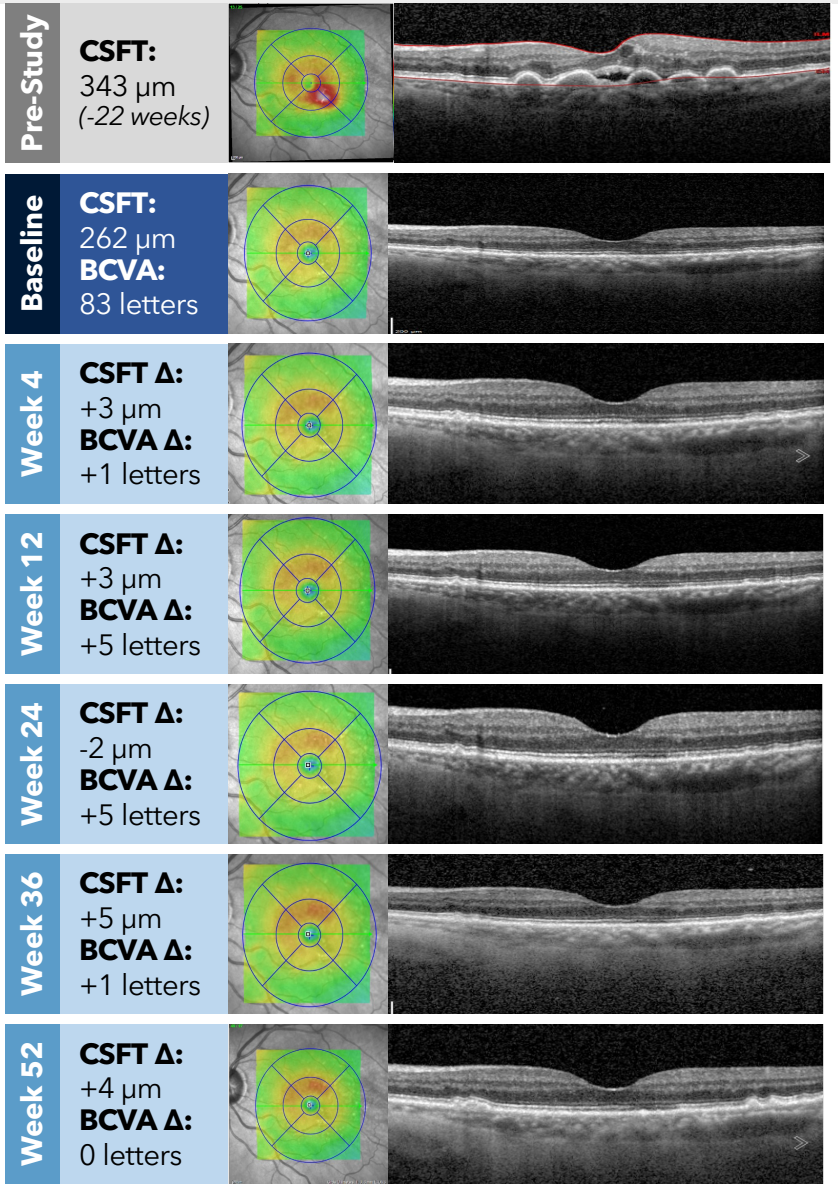


BCVA (Best Corrected Visual Acuity); CSFT (Central Subfield Thickness)

Case Example: OTX-TKI Reduces Fluctuation in Fluid and CSFT for 1 Year

80yo female with aflibercept q4-8W prior to study and rescue-free through 1 year





BCVA (Best Corrected Visual Acuity); CSFT (Central Subfield Thickness)

Phase 1 Clinical Trials for nAMD Indicates Durability and Biological Activity of OTX-TKI

OTX-TKI reduced vascular leakage following VEGF challenge in a rabbit study demonstrating rapid and sustained axitinib tissue levels

Phase 1 Australia Clinical Trial

Observed reductions in CSFT throughout 12 months in treatment-naïve, monotherapy subjects

Phase 1 US Clinical Trial

No reports of drug-related ocular or systemic SAEs in either arm

89% reduction in anti-VEGF treatment burden observed for OTX-TKI subjects at 52 weeks

Changes in BCVA and CSFT were similar to the standard-of-care, aflibercept 2mg Q8W arm

Anatomic outcomes support hypothesis that a single injection of OTX-TKI in nAMD patients may achieve durability between 6-12 months

BCVA (Best corrected visual acuity); CSFT (Central subfield thickness); nAMD (Neovascular age-related macular degeneration); SAE (Serious adverse event); VEGF (Vascular endothelial growth factor). ; nAMD (neovascular age-related macular degeneration)

Thank you.