Redefining the Management of nAMD

The Impact of Durability and Sustained Disease Control

November 7, 2026

OSN New York | New York, NY

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Any statements in this presentation about future expectations, plans, and prospects for the Company, including statements regarding the development and regulatory status of the Company's or its competitors' product candidates, including statements regarding the SOL-1 Phase 3 superiority trial being conducted under a Special Protocol Assessment (SPA) agreement with the U.S. FDA and aligned with FDA draft guidance for neovascular AMD drug development; the timing, design, enrollment, randomization, conduct and retention of subjects in the Company's clinical trials, including the Company's SOL-1 trial and its SOL-R Phase 3 non-inferiority trial and SOL-X open-label extension trial of OTX-TKI for the treatment of wet age-related macular degeneration (wet AMD), also known as neovascular age-related macular degeneration (nAMD); statements regarding the potential utility or adoption of OTX-TKI or its competitors, if approved; statements regarding the Company's intention to submit a new drug application for OTX-TKI, based on data from the Company's SOL-1 trial in wet AMD, subject to planned formal discussions with the FDA; and other statements containing the words "anticipate", "become", "believe", "estimate", "expect", "intend", "designed", "goal", "may", "might", "plan", "position", "predict", "project", "target", "potential", "will", "would", "could", "should", "continue", and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. 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- **Consultant:** Alcon, Annexon, Apellis, Astellas, Bausch + Lomb, Ocular Therapeutix, Pr3vent, Valitor, Regeneron
- **Stock/Stock options:** Ocular Therapeutix, Pr3vent, Valitor

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Disclaimer

The following presentation discusses OTX-TKI - an investigational product candidate that has not been approved by the FDA or any other regulatory body; safety and effectiveness have not been established

Agenda

Therapeutic Advances, Yet Unmet Need Remains
Andrew A. Moshfeghi MD, MBA, FASRS

OTX-TKI: Scientific Rationale and Primary SOL-1 Findings
Dilsher S. Dhoot MD, FASRS

SOL-1: Insights Into Treatment Response
Yasha S. Modi MD, MHS

Clinical Insights Through Patient Cases
Mark R. Barakat MD, FASRS

Driving Clinical Development Through Evidence-Based Strategy
Jeffrey S. Heier MD, FASRS

Panel Discussion

Therapeutic Advances, Yet Unmet Need Remains

Andrew A. Moshfeghi MD, MBA, FASRS



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Treatment Burden Remains a Significant Unmet Need in nAMD

INJECTION BURDEN

up to
12 anti-VEGF injections/yr for patients[1]



90% of patients require injection **every 1-3 months**[2]

up to
12 days off/yr for patients and caregivers



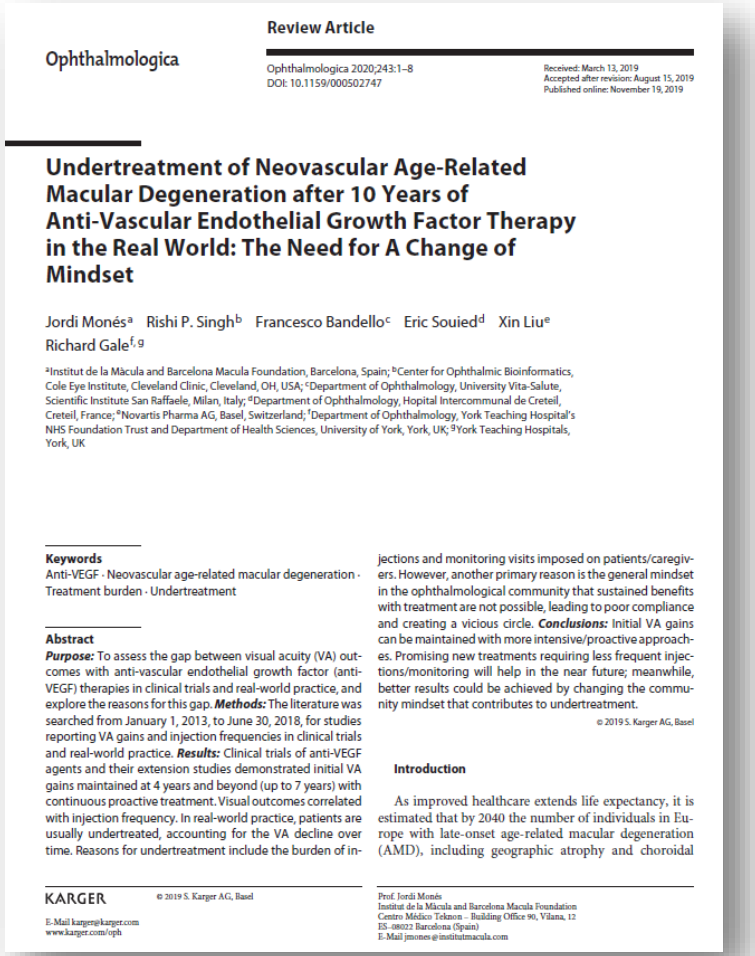
Frequent injections and visits **disrupt patients' daily routines** and activities[3]

40% discontinue treatment in the first year due to heavy treatment burden[4]

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1. MacCumber MW, et al. *Can J Ophthalmol*. 2023;58(3):252-261. 2. Ophthalmic Market Trends: Quarterly US Retina Edition: Q3-2024 Analysis of Historical Trends and Latest Developments. Market Scope; 2024. 3. Varano M, et al. *Clin Ophthalmol.* 2016;10:257-267. 4. Khanani AM, et al. *Ophthalmology Retina*. 2020;4(2):122-133.
nAMD, neovacular age-related macular degeneration

Suboptimal Frequency of Injections Contribute to Declining Real-World Outcomes



Ophthalmologica

Review Article

Ophthalmologica 2020;243:1–8
DOI: 10.1159/000502747

Received: March 13, 2019
Accepted after revision: August 15, 2019
Published online: November 19, 2019

Undertreatment of Neovascular Age-Related Macular Degeneration after 10 Years of Anti-Vascular Endothelial Growth Factor Therapy in the Real World: The Need for A Change of Mindset

Jordi Monés[a] Rishi P. Singh[b] Francesco Bandello[c] Eric Souied[d] Xin Liu[e] Richard Gale[f, g]

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Keywords
Anti-VEGF · Neovascular age-related macular degeneration · Treatment burden · Undertreatment

Abstract
Purpose: To assess the gap between visual acuity (VA) outcomes with anti-vascular endothelial growth factor (anti-VEGF) therapies in clinical trials and real-world practice, and explore the reasons for this gap. ***Methods:*** The literature was searched from January 1, 2013, to June 30, 2018, for studies reporting VA gains and injection frequencies in clinical trials and real-world practice. ***Results:*** Clinical trials of anti-VEGF agents and their extension studies demonstrated initial VA gains maintained at 4 years and beyond (up to 7 years) with continuous proactive treatment. Visual outcomes correlated with injection frequency. In real-world practice, patients are usually undertreated, accounting for the VA decline over time. Reasons for undertreatment include the burden of injections and monitoring visits imposed on patients/caregivers. However, another primary reason is the general mindset in the ophthalmological community that sustained benefits with treatment are not possible, leading to poor compliance and creating a vicious circle. ***Conclusions:*** Initial VA gains can be maintained with more intensive/proactive approaches. Promising new treatments requiring less frequent injections/monitoring will help in the near future; meanwhile, better results could be achieved by changing the community mindset that contributes to undertreatment.

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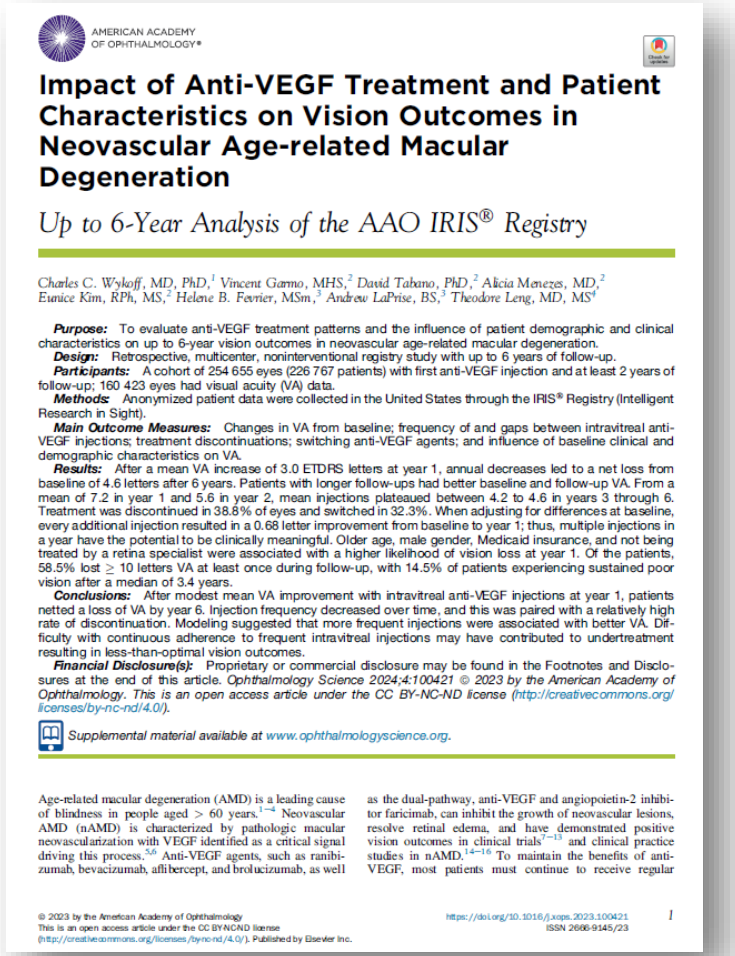
Introduction

As improved healthcare extends life expectancy, it is estimated that by 2040 the number of individuals in Europe with late-onset age-related macular degeneration (AMD), including geographic atrophy and choroidal

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Impact of Anti-VEGF Treatment and Patient Characteristics on Vision Outcomes in Neovascular Age-related Macular Degeneration

Up to 6-Year Analysis of the AAO IRIS® Registry

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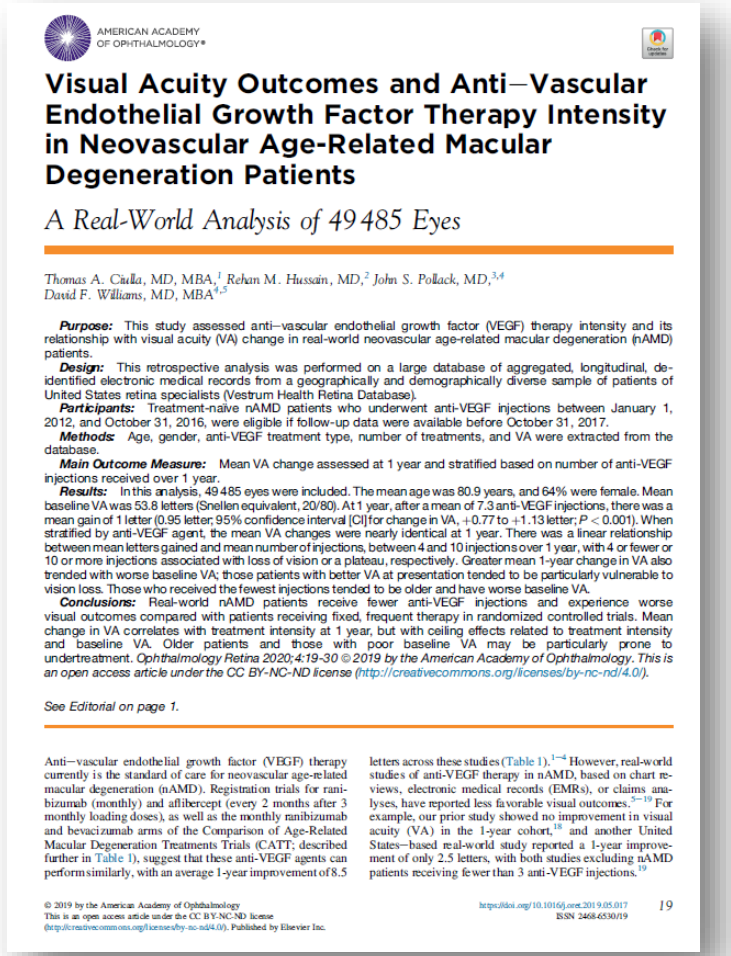
Purpose: To evaluate anti-VEGF treatment patterns and the influence of patient demographic and clinical characteristics on up to 6-year vision outcomes in neovascular age-related macular degeneration.
Design: Retrospective, multicenter, noninterventional registry study with up to 6 years of follow-up.
Participants: A cohort of 254 655 eyes (226 767 patients) with first anti-VEGF injection and at least 2 years of follow-up; 160 423 eyes had visual acuity (VA) data.
Methods: Anonymized patient data were collected in the United States through the IRIS® Registry (Intelligent Research in Sight).
Main Outcome Measures: Changes in VA from baseline; frequency of and gaps between intravitreal anti-VEGF injections; treatment discontinuations; switching anti-VEGF agents; and influence of baseline clinical and demographic characteristics on VA.
Results: After a mean VA increase of 3.0 ETDRS letters at year 1, annual decreases led to a net loss from baseline of 4.6 letters after 6 years. Patients with longer follow-ups had better baseline and follow-up VA. From a mean of 7.2 in year 1 and 5.6 in year 2, mean injections plateaued between 4.2 to 4.6 in years 3 through 6. Treatment was discontinued in 38.8% of eyes and switched in 32.3%. When adjusting for differences at baseline, every additional injection resulted in a 0.68 letter improvement from baseline to year 1; thus, multiple injections in a year have the potential to be clinically meaningful. Older age, male gender, Medicaid insurance, and not being treated by a retina specialist were associated with a higher likelihood of vision loss at year 1. Of the patients, 58.5% lost ≥ 10 letters VA at least once during follow-up, with 14.5% of patients experiencing sustained poor vision after a median of 3.4 years.
Conclusions: After modest mean VA improvement with intravitreal anti-VEGF injections at year 1, patients netted a loss of VA by year 6. Injection frequency decreased over time, and this was paired with a relatively high rate of discontinuation. Modeling suggested that more frequent injections were associated with better VA. Difficulty with continuous adherence to frequent intravitreal injections may have contributed to undertreatment resulting in less-than-optimal vision outcomes.
Financial Disclosure(s): Proprietary or commercial disclosure may be found in the Footnotes and Disclosures at the end of this article. *Ophthalmology Science 2024;4:100421 © 2023 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

Supplemental material available at www.ophthalmologyscience.org.

Age-related macular degeneration (AMD) is a leading cause of blindness in people aged > 60 years.[1–4] Neovascular AMD (nAMD) is characterized by pathologic macular neovascularization with VEGF identified as a critical signal driving this process.[5,6] Anti-VEGF agents, such as ranibizumab, bevacizumab, aflibercept, and brolucizumab, as well as the dual-pathway, anti-VEGF and angiopoietin-2 inhibitor faricimab, can inhibit the growth of neovascular lesions, resolve retinal edema, and have demonstrated positive vision outcomes in clinical trials[7–13] and clinical practice studies in nAMD.[14–16] To maintain the benefits of anti-VEGF, most patients must continue to receive regular

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https://doi.org/10.1016/j.xops.2023.100421
ISSN 2666-9145/23



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Visual Acuity Outcomes and Anti–Vascular Endothelial Growth Factor Therapy Intensity in Neovascular Age-Related Macular Degeneration Patients

A Real-World Analysis of 49 485 Eyes

Thomas A. Ciulla, MD, MBA,[1] Rehan M. Hussain, MD,[2] John S. Pollack, MD,[3,4] David F. Williams, MD, MBA[4,5]

Purpose: This study assessed anti–vascular endothelial growth factor (VEGF) therapy intensity and its relationship with visual acuity (VA) change in real-world neovascular age-related macular degeneration (nAMD) patients.
Design: This retrospective analysis was performed on a large database of aggregated, longitudinal, de-identified electronic medical records from a geographically and demographically diverse sample of patients of United States retina specialists (Vestrum Health Retina Database).
Participants: Treatment-naive nAMD patients who underwent anti-VEGF injections between January 1, 2012, and October 31, 2016, were eligible if follow-up data were available before October 31, 2017.
Methods: Age, gender, anti-VEGF treatment type, number of treatments, and VA were extracted from the database.
Main Outcome Measure: Mean VA change assessed at 1 year and stratified based on number of anti-VEGF injections received over 1 year.
Results: In this analysis, 49 485 eyes were included. The mean age was 80.9 years, and 64% were female. Mean baseline VA was 53.8 letters (Snellen equivalent, 20/80). At 1 year, after a mean of 7.3 anti-VEGF injections, there was a mean gain of 1 letter (0.95 letter; 95% confidence interval [CI] for change in VA, +0.77 to +1.13 letter; $P < 0.001$). When stratified by anti-VEGF agent, the mean VA changes were nearly identical at 1 year. There was a linear relationship between mean letters gained and mean number of injections, between 4 and 10 injections over 1 year, with 4 or fewer or 10 or more injections associated with loss of vision or a plateau, respectively. Greater mean 1-year change in VA also trended with worse baseline VA; those patients with better VA at presentation tended to be particularly vulnerable to vision loss. Those who received the fewest injections tended to be older and have worse baseline VA.
Conclusions: Real-world nAMD patients receive fewer anti-VEGF injections and experience worse visual outcomes compared with patients receiving fixed, frequent therapy in randomized controlled trials. Mean change in VA correlates with treatment intensity at 1 year, but with ceiling effects related to treatment intensity and baseline VA. Older patients and those with poor baseline VA may be particularly prone to undertreatment. *Ophthalmology Retina 2020;4:19-30 © 2019 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

See Editorial on page 1.

Anti–vascular endothelial growth factor (VEGF) therapy currently is the standard of care for neovascular age-related macular degeneration (nAMD). Registration trials for ranibizumab (monthly) and aflibercept (every 2 months after 3 monthly loading doses), as well as the monthly ranibizumab and bevacizumab arms of the Comparison of Age-Related Macular Degeneration Treatments Trials (CATT; described further in Table 1), suggest that these anti-VEGF agents can perform similarly, with an average 1-year improvement of 8.5 letters across these studies (Table 1).[1–4] However, real-world studies of anti-VEGF therapy in nAMD, based on chart reviews, electronic medical records (EMRs), or claims analyses, have reported less favorable visual outcomes.[5–19] For example, our prior study showed no improvement in visual acuity (VA) in the 1-year cohort,[18] and another United States–based real-world study reported a 1-year improvement of only 2.5 letters, with both studies excluding nAMD patients receiving fewer than 3 anti-VEGF injections.[19]

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https://doi.org/10.1016/j.oret.2019.05.017
ISSN 2468-6530/19

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1. Monés J, et al. *Ophthalmologica*. 2020;243(1):1-8. 2. Wykoff CC, et al. *Ophthalmol Sci*. 2023;4(2):100421. 3. Ciulla TA, et al. *Ophthalmol Retina*. 2020;4(1):19–30.

How Far Have We Extended Treatment?

DRUG / TRIAL	INTERVAL STUDIED	% ACHIEVING INTERVAL	TRIAL TYPE
Ranibizumab 0.5 mg MARINA / ANCHOR[1,2]	Every 4 weeks	FIXED REGIMEN	SUPERIORITY
Aflibercept 2 mg VIEW1 / VIEW2[3]	Every 4-8 weeks	FIXED REGIMEN	Non-inferiority
Brolucizumab 6 mg HAWK / HARRIER[4]	Up to 12 weeks	~56%	Non-inferiority
Faricimab TENAYA / LUCERNE[5]	Up to 16 weeks	~46%	Non-inferiority
Aflibercept 8 mg PULSAR[6]	Up to 16 weeks	~77%	Non-inferiority
Ranibizumab Port Delivery System ARCHWAY[7]	Every 24 weeks	~98%	Non-inferiority
OTX-TKI SOL-1	**36 weeks** **52 weeks**	**~75% supplemental-free** **~69% supplemental-free**	**SUPERIORITY**

The data presented here include a comparison of results from distinct clinical trials. These studies featured varying inclusion and exclusion criteria, baseline characteristics, and patient demographics which may significantly impact clinical outcomes. Because comparisons between these trials may not be generalizable, this overview is for informational purposes only and does not constitute a head-to-head evaluation or definitive proof of relative therapeutic value.

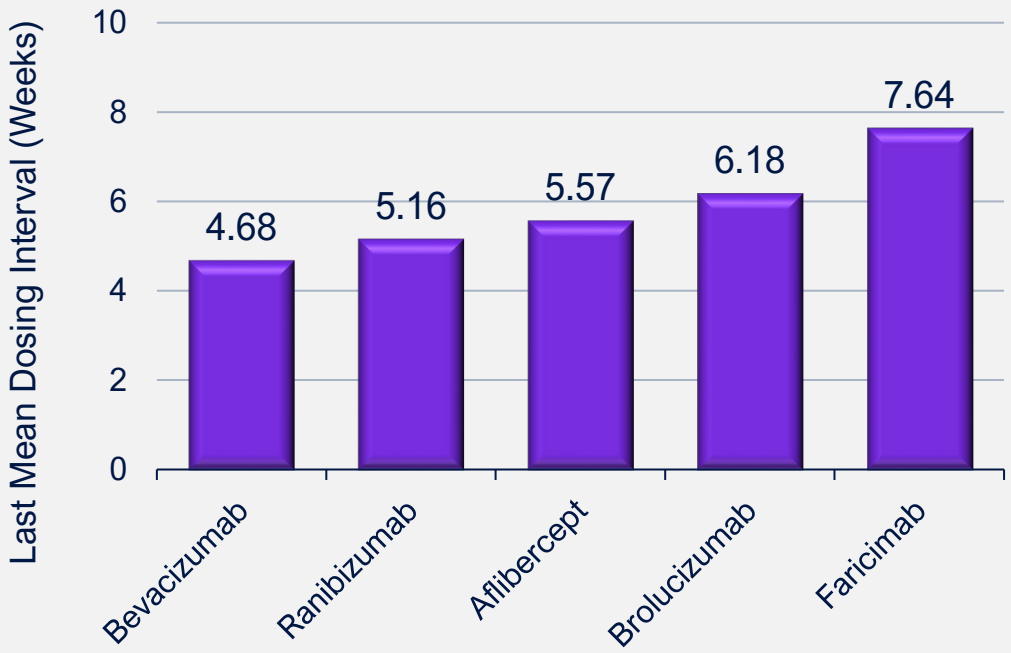
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SOL-1: Supplemental-free subjects include those who did not require rescue injections as specified by the protocol.

1. Rosenfeld PJ, et al. *N Engl J Med*. 2006;355(14):1419–1431. 2. Brown DM, et al. *N Engl J Med*. 2006;355(14):1432–1444. 3. Heier JS, et al. *Ophthalmology*. 2012;119(12):2537–2548. 4. Dugel PU, et al. *Ophthalmology*. 2020;127(1):72–84. 5. Heier JS, et al. *Lancet*. 2022;399(10326):729–740. 6. Lanzetta P, et al. *Lancet*. 2024;403(10432):1141–1152. 7. Holekamp NM, et al. *Ophthalmology*. 2022;129(3):295–307.

Second Generation nAMD Agents Extend Injection Intervals Incrementally Over Previous Agents in the Real World

Comparison of Intravitreal Injection Intervals (n=190)[1*]



Real World Use of Aflibercept 8 mg: IRIS Registry Data[2†]

Group	Achieved Interval
Treatment-naïve (n=1361)	Median **12 weeks**
Switchers (n=8311)	**~73% at ≤10 weeks** after switch from 2 mg to 8 mg

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*Retrospective, real-world study of 190 eyes with nAMD previously treated with anti-VEGF therapy and received ≥3 intravitreal faricimab injections with ≥3 months follow-up.
†Retrospective real-world analysis using the IRIS Registry of eyes with nAMD or DME initiating aflibercept 8mg or switching from aflibercept 2mg to 8mg during the indexing period. Information presented herein reflects nAMD cohort (n=9672 eyes)
1. Leung EH, et al. *Clin Ophthalmol*. 2023;17:1287-1293. 2. Do DV, et al. Real-world use of aflibercept 8 mg in nAMD or DME: IRIS® Registry analysis. Presented at: AAO Retina Subspecialty Day; Oct 17–18, 2025; Palo Alto, CA.
nAMD, neovascular age-related macular degeneration; IRIS, Intelligent Research in Sight

Existing Literature Underestimates True Attrition in nAMD

Themes in Attrition Literature

Varying Definitions of Discontinuation

Ranging from **6-12 Months**

Strict Inclusion Criteria Limit Relevance

Prior registry analyses required 1.5 & 2 years of **follow-up**

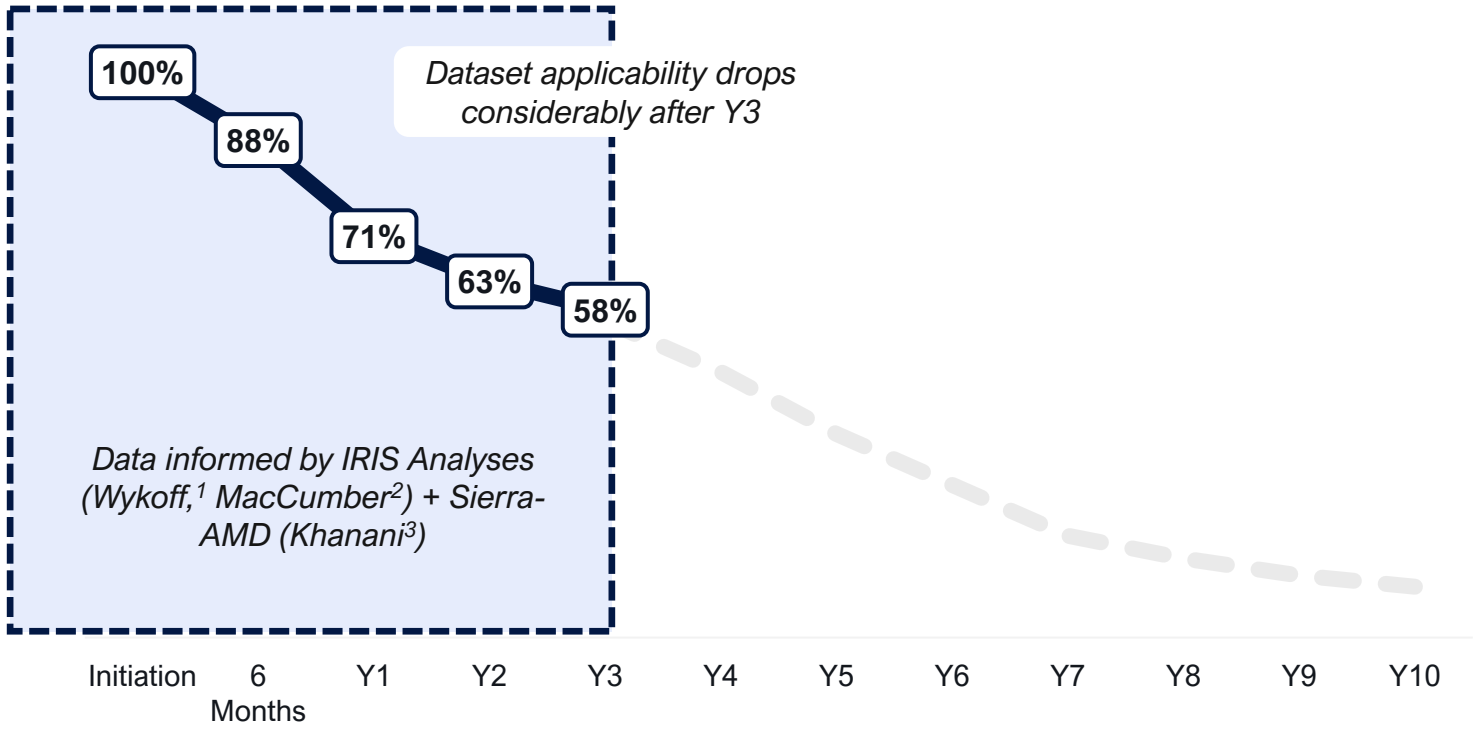
Limited Longer-Term Follow-Up

Large studies **rarely follow patients** beyond first **2-3 years**

Attrition appeared to be a secondary focus

in large registry analyses with anti-VEGFs in nAMD

Literature-Based Attrition Curve*



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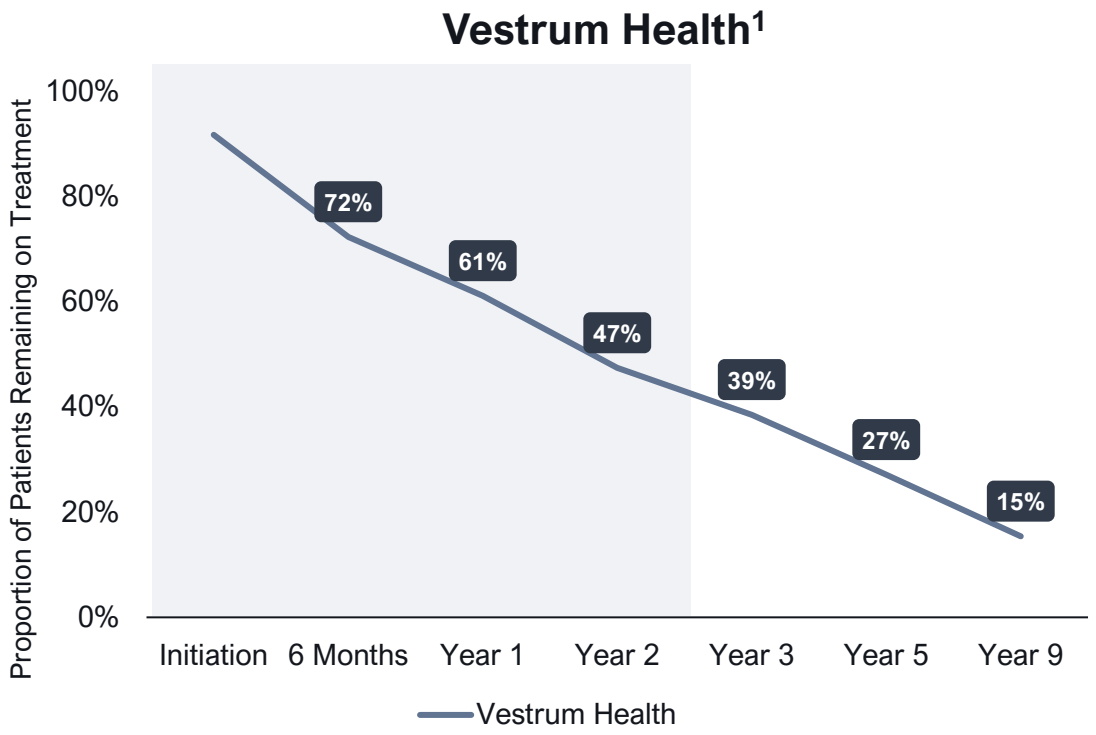
*Literature-Based Attrition Curve generated by Ocular Therapeutix by analysis of references 1-3. Trend line following Year 3 is illustrative and based on decline shown in in Years 1-3

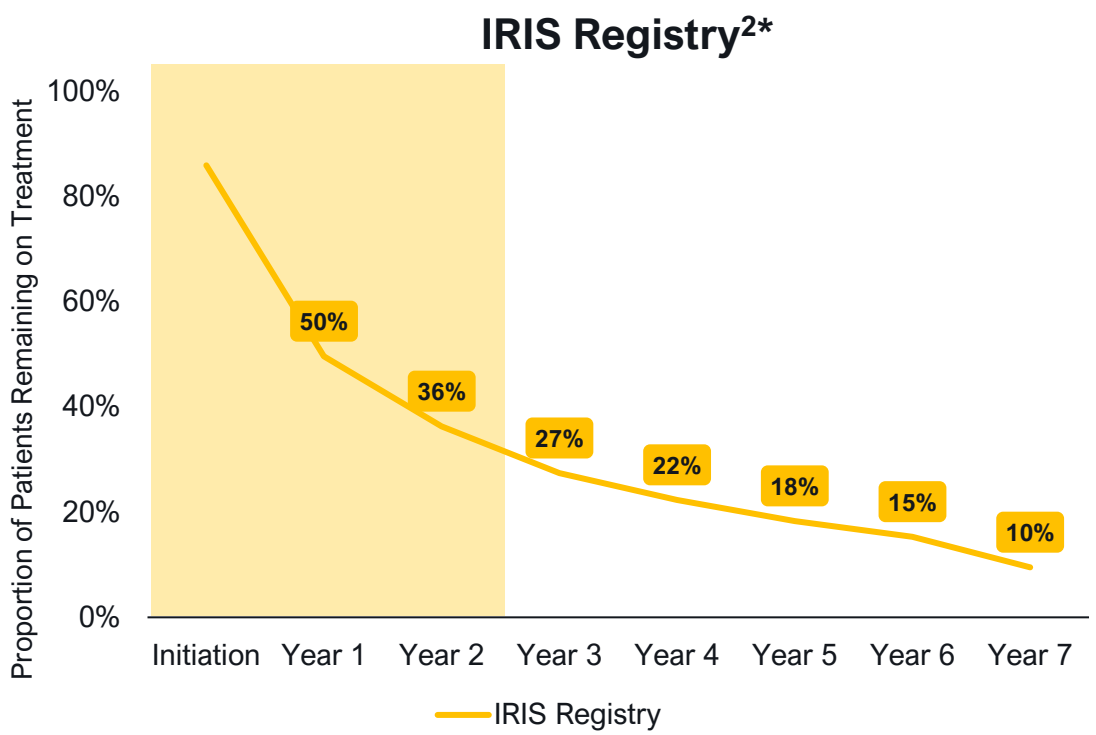
1. Wykoff CC, et al. *Ophthalmol Sci*. 2023;4(2):100421. 2. MacCumber MW, et al. *Can J Ophthalmol*. 2023;58(3):252-261. 3. Khanani AM, et al. *Ophthalmol Retina*. 2020;4(2):122-133.

nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.

High Real-World Discontinuation Highlights Unmet Need for Durable, Low-Burden nAMD Therapy

Steepest Drop-Off in Years 1–2; Continued Decline Through Years 3–7+



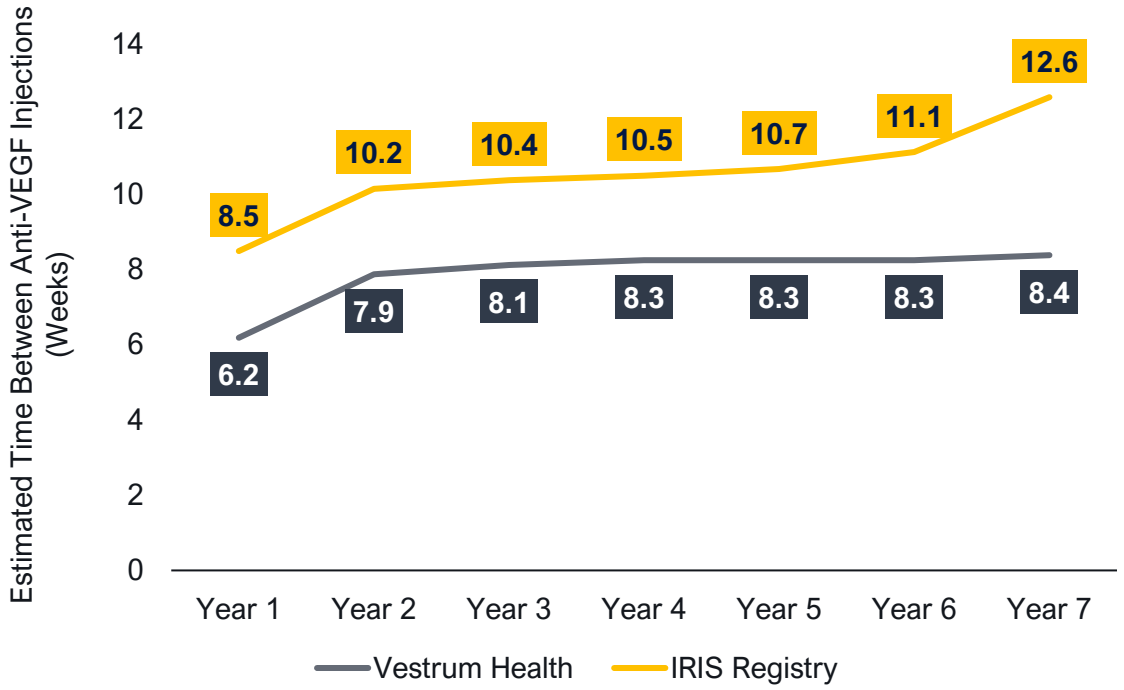


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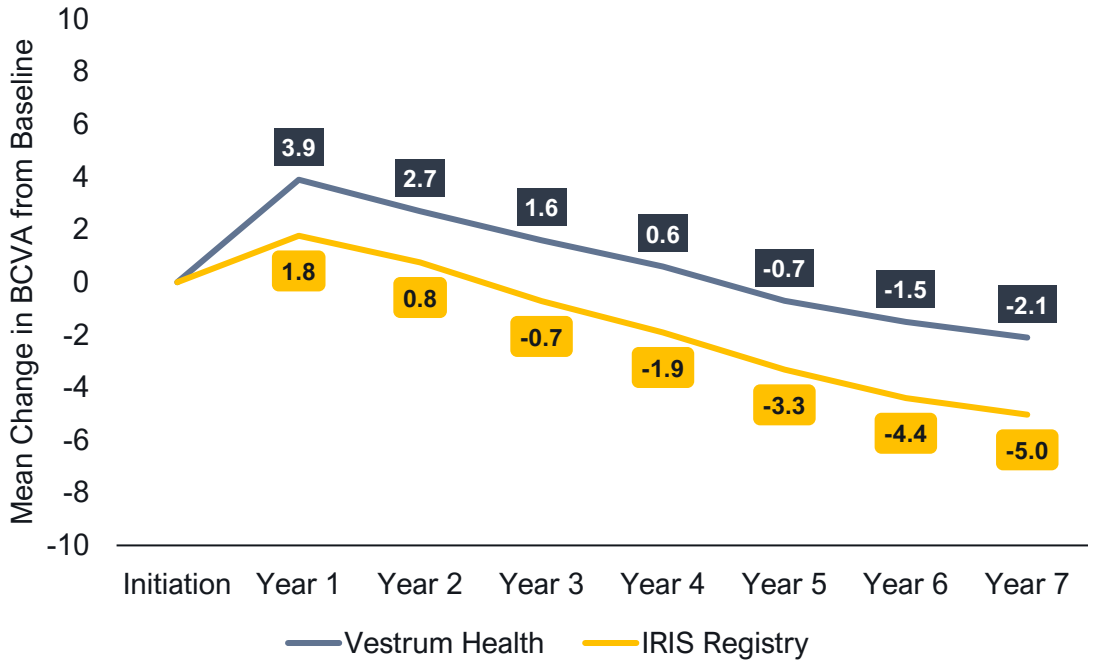
*Cohort with the longest observation period for IRIS Registry with 67,156 eyes
Time to discontinuation was defined as > 6 months without anti-VEGF
1. Data on File 048. Ocular Therapeutix. 2026. 2. Data on File 047. Ocular Therapeutix. 2026.
IRIS, Intelligent Research in Sight

Real-World Anti-VEGF Use Shows As Treatment Intervals Increase, Visual Acuity Decreases

Treatment Interval in Weeks



Long-Term Visual Outcomes*



Treatment-Free Interval Increases Over Time in Both Databases
Vestrum Health increases from 6.2 weeks in Year 1 to 8.4 weeks by Year 7
IRIS Registry increases from 8.5 weeks at Year 1 to 12.6 weeks by Year 7

Both Databases Show Early Gains Followed by Long-Term Decline
Vestrum Health: +3.9 letters at Year 1 to −2.1 by Year 7
IRIS Registry: +1.8 letters at Year 1 to −5.0 by Year 7

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Data on File, Ocular Therapeutix
*Visual outcomes: mean change from baseline in ETDRS letters

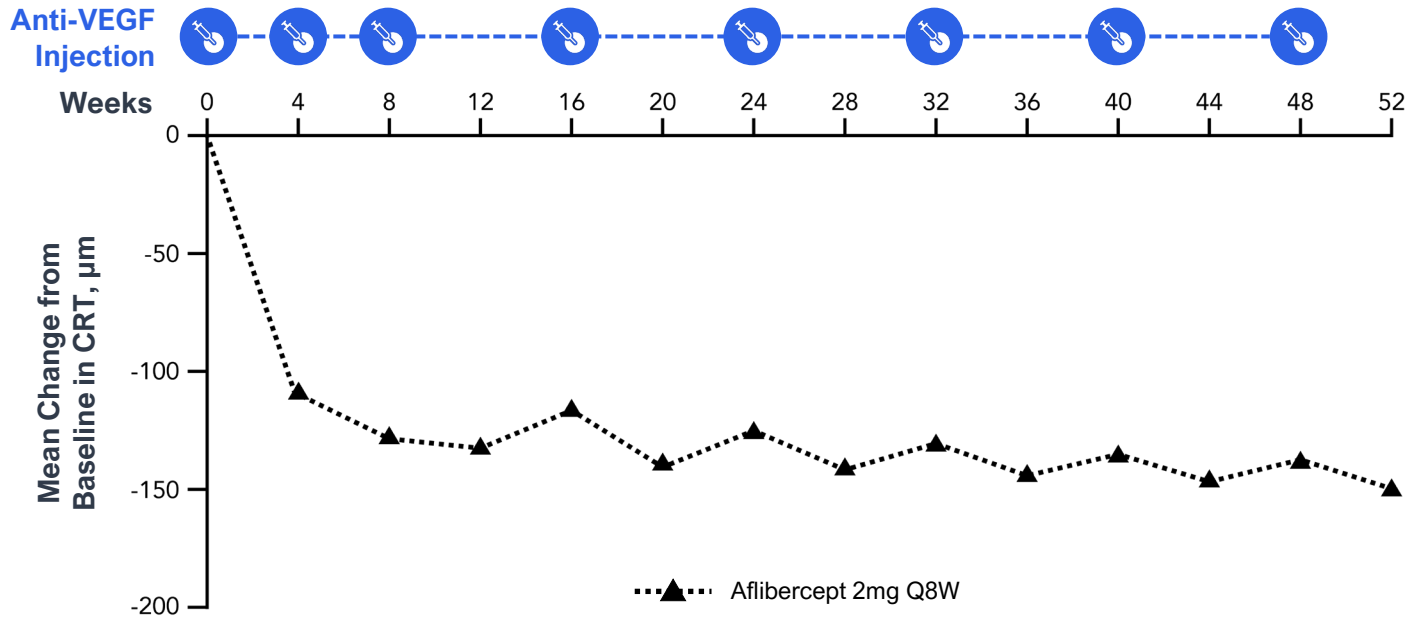
Greater Retinal Thickness Variability During Anti-VEGF Therapy is Associated with Suboptimal Anatomic and Visual Outcomes

Retinal Thickness Fluctuations

Development of Fibrosis and Atrophy

Poorer Long-Term Visual Outcomes

Repeated cycles of fluid resolution and recurrence are reflected in fluctuations in retinal thickness over time



OCULAR THERAPEUTIX Retina experience redefined

Figure adapted from Heier JS, et al. *Ophthalmology*. 2012;119(12):2537-2548.
VIEW 1 and VIEW 2 were similarly designed, randomized, double-masked, active-controlled Phase 3 trials in patients with nAMD (N=2419) comparing aflibercept dosing regimens with ranibizumab Q4W; figure illustrates mean CRT change through Week 52 with aflibercept 2mg Q8W following 3 monthly doses.
CRT, central retinal thickness; nAMD, neovascular age-related macular degeneration; Q, every; VEGF, vascular endothelial growth factor; W, week

Greater Retinal Thickness Variability During Anti-VEGF Therapy is Associated with Suboptimal Anatomic and Visual Outcomes

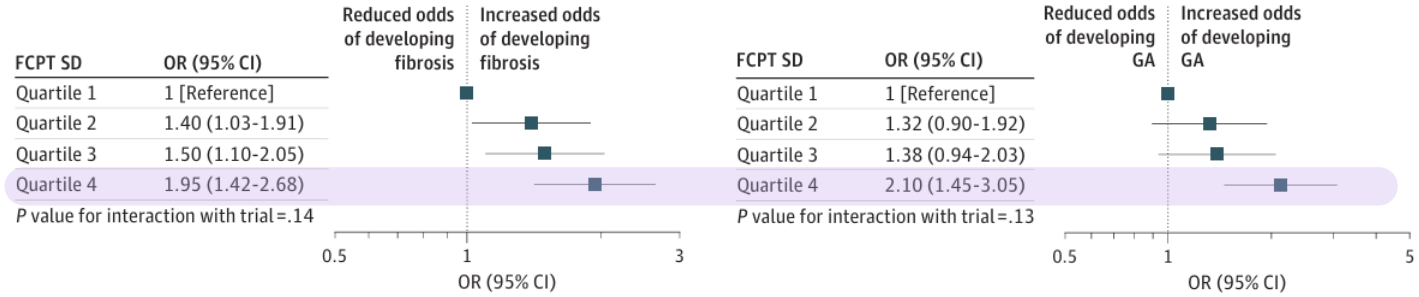
Retinal Thickness Fluctuations

Development of Fibrosis and Atrophy

Poorer 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



In a post hoc analysis, highest retinal thickness variability had approximately **double the odds** of developing fibrosis/macular atrophy

OCULAR THERAPEUTIX Retina experience redefined™

Post hoc analysis of 1731 previously untreated nAMD eyes from CATT (Comparison of Age-Related Macular Degeneration Treatment Trials) and IVAN (Inhibition of VEGF in Age-related Choroidal Neovascularization) randomized trials. Retinal thickness variability was defined as the SD of FCPT measurements and categorized into quartiles. Adjusted analyses evaluated associates with BCVA, development of fibrosis, and development of macular atrophy at Month 24 or the last available visit.

Evans RN, et al. *JAMA Ophthalmol*. 2020;138(10):1043-1051.

BCVA, best-corrected visual acuity; CI, confidence interval; FCPT, foveal center-point thickness; GA, geographic atrophyOR, odds ratio; VEGF, vascular endothelial growth factor; SD, standard deviation

Greater Retinal Thickness Variability During Anti-VEGF Therapy is Associated with Suboptimal Anatomic and Visual Outcomes

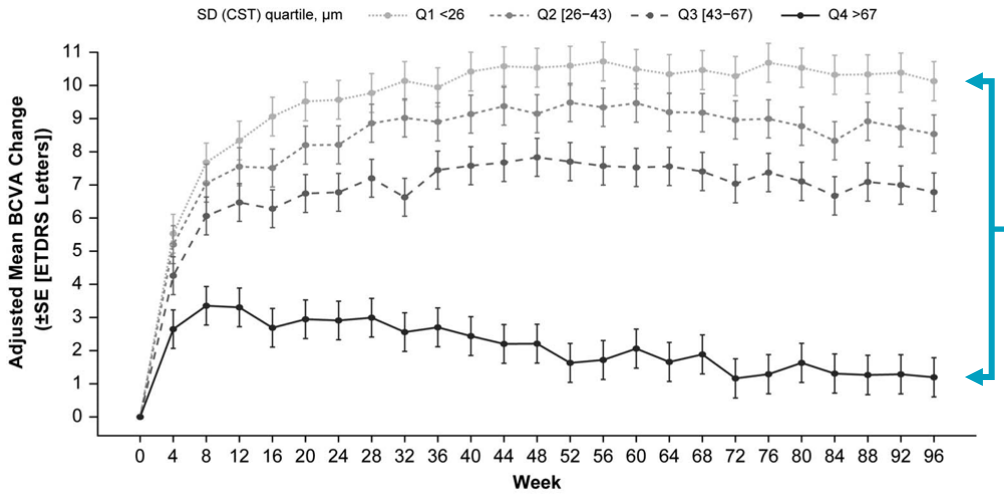
Retinal Thickness Fluctuations

Development of Fibrosis and Atrophy

Poorer Long-Term Visual Outcomes

EFFECT OF RETINAL THICKNESS VARIABILITY ON VISUAL OUTCOMES AND FLUID PERSISTENCE IN NEOVASCULAR AGE-RELATED MACULAR DEGENERATION

A Post Hoc Analysis of the HAWK and HARRIER Studies



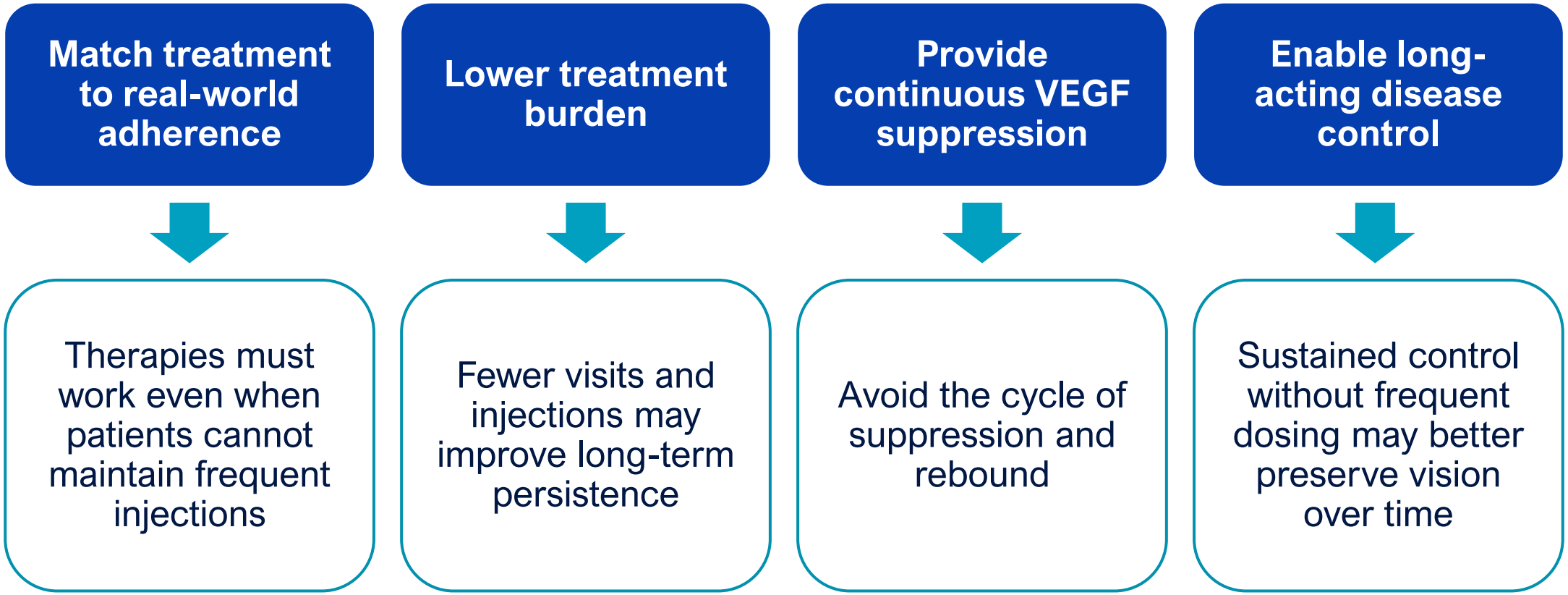
Vision deteriorates by ~9 letters between patients with most and least stable retinal thicknesses

Post hoc, treatment-agnostic analysis of pooled HAWK and HARRIER data from 1752 patients with nAMD treated with brolucizumab or aflibercept. Patients were categorized into quartiles based on the SD of CST measurements from baseline through Week 96, and adjusted BCVA change was evaluated using a repeated measure model.

Dugel PU, et al. *Retina*. 2022;42(3):511-518.

BCVA, best-corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; SE, standard error; SD, standard devliation; Q, quartiles

Redefining nAMD Therapy: What can we do better?



OCULAR THERAPEUTIX Retina experience redefined

nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor

OTX-TKI: Scientific Rationale and Primary SOL-1 Findings

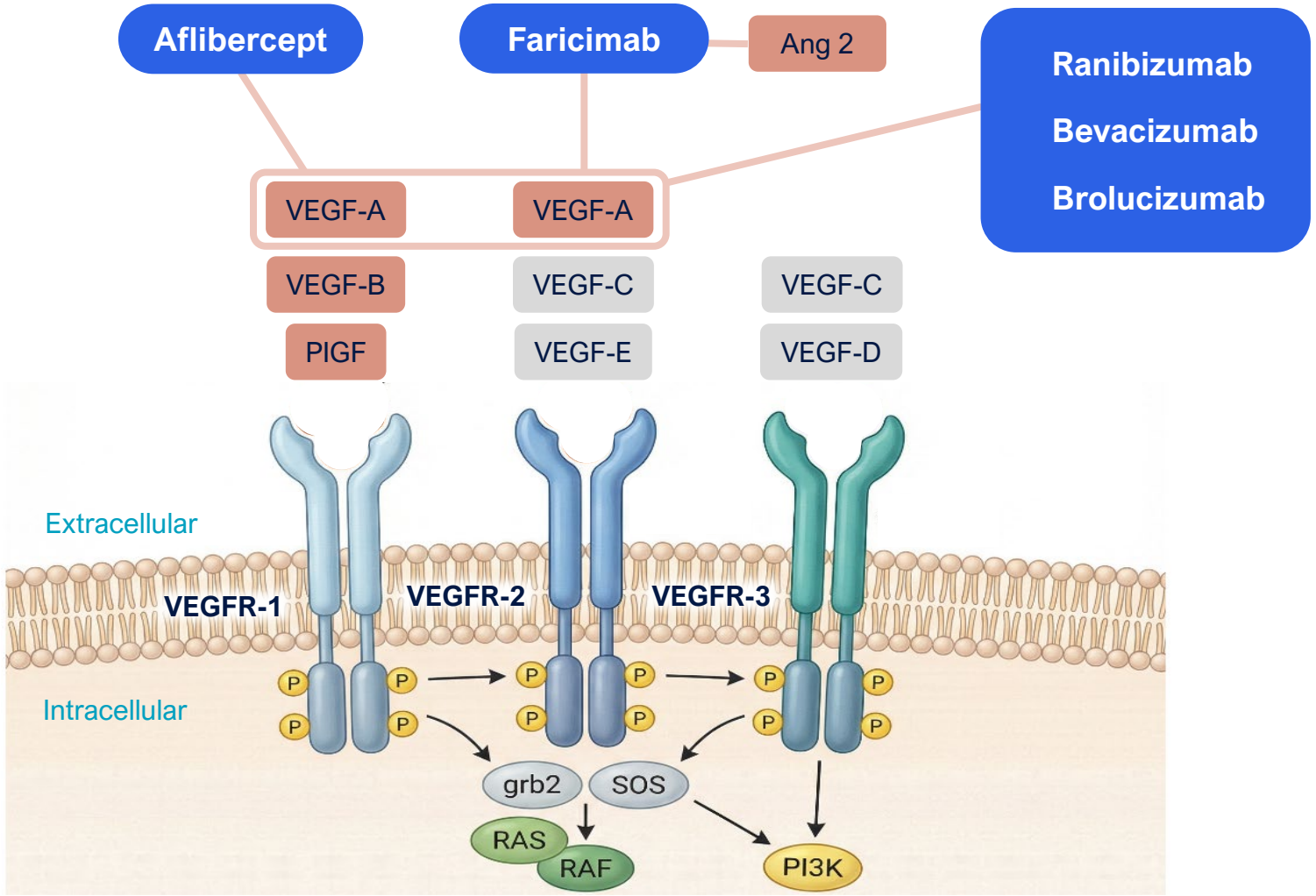
Dilsher S. Dhoot MD, FASRS

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Retina experience redefined

Current Anti-VEGF Therapies Selectively Target Only Extracellular VEGF

Current **Anti-VEGF** agents act **extracellularly by binding selective ligands**, like VEGF-A, preventing receptor binding and activation[1,2]



Select extracellular target binding of VEGF, PlGF and Ang-II to inhibit angiogenesis. Adapted from Zhao et al. 2015.[2-4]

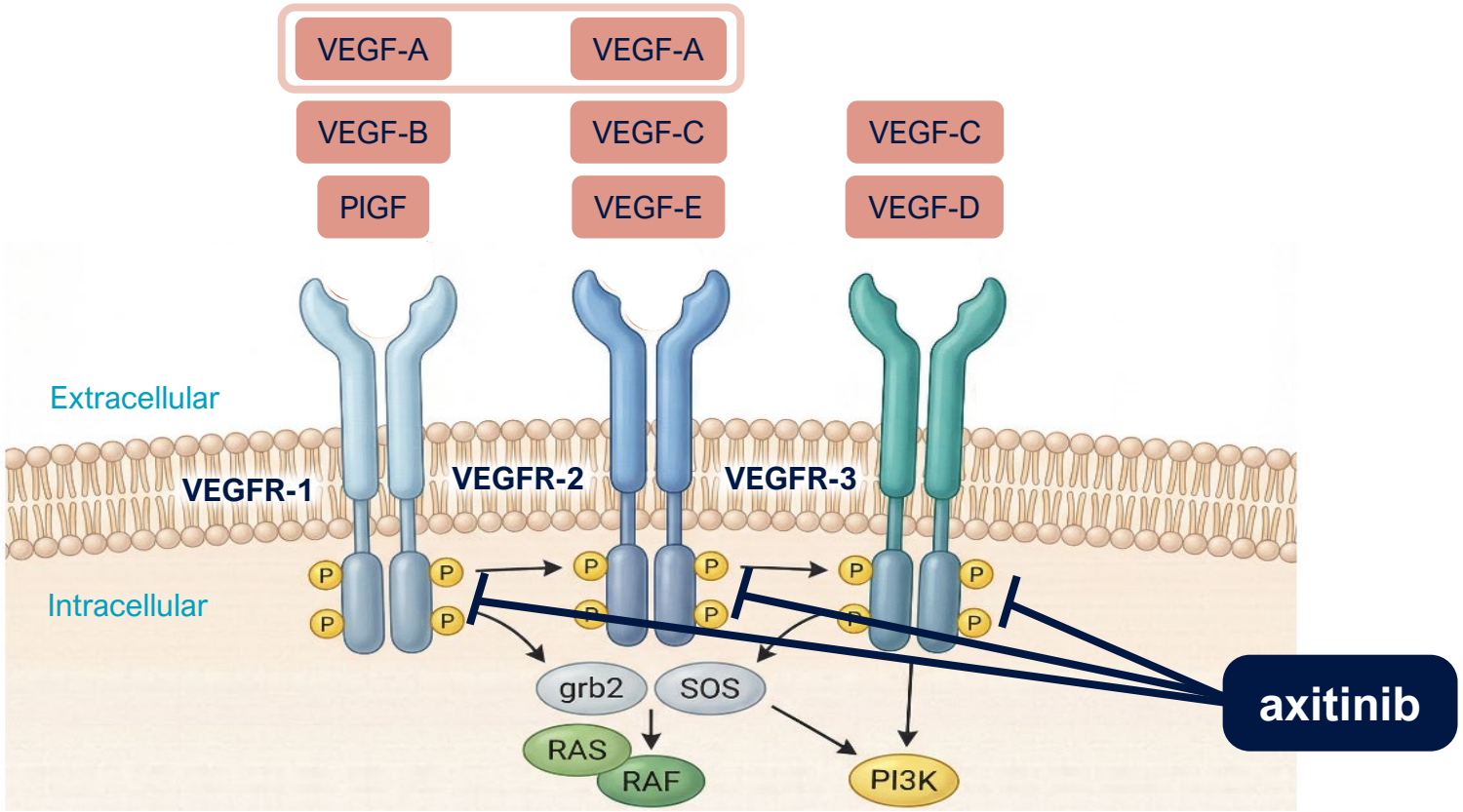
OCULAR THERAPEUTIX Retina experience redefined™

1. Hu-Lowe DD, et al. *Clin Cancer Res*. 2008;14(22):7272-7283. 2. Zhao Y, et al. *Oncologist*. 2015;20(6):660-673. 3. Tan CS, et al. *Clin Ophthalmol*. 2022;16:917-933. 4. Khachigian LM, et al. *J Transl Med*. 2023;21(1):133.

PlGF, placenta growth factor; VEGF(R), vascular endothelial growth factor (receptor); P, phosphate; grb2, growth factor receptor-bound protein 2; SOS, son of sevenless; RAS, rat sarcoma viral oncogene homolog; RAF, rapidly accelerated fibrosarcoma; PI3K, phosphatidylinositol 3-kinase; TKI, tyrosine kinase inhibitor; Ang 2, angiopoietin-2

Tyrosine Kinase Inhibitors Act Intracellularly to Inhibit Receptor Signaling

Tyrosine Kinase Inhibitors (TKI) bind at the **intracellular tyrosine kinase domains** of VEGF receptors, inhibiting ATP binding and preventing activation of pro-angiogenic signaling[1,2]



Select angiogenesis intracellular targets of inhibition for tyrosine kinase inhibitors. Adapted from Zhao et al. 2015.[2-4]

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1. Hu-Lowe DD, et al. *Clin Cancer Res*. 2008;14(22):7272-7283. 2. Zhao Y, et al. *Oncologist*. 2015;20(6):660-673. 3. Tan CS, et al. *Clin Ophthalmol*. 2022;16:917-933. 4. Khachigian LM, et al. *J Transl Med*. 2023;21(1):133.

PlGF, placenta growth factor; VEGF(R), vascular endothelial growth factor (receptor); P, phosphate; grb2, growth factor receptor-bound protein 2; SOS, son of sevenless; RAS, rat sarcoma viral oncogene homolog; RAF, rapidly accelerated fibrosarcoma; PI3K, phosphatidylinositol 3-kinase; TKI, tyrosine kinase inhibitor.

OTX-TKI: Axitinib via Hydrogel Allows for Tunable Sustained Release

AXITINIB

Multi-target Tyrosine Kinase Inhibitor (TKI)

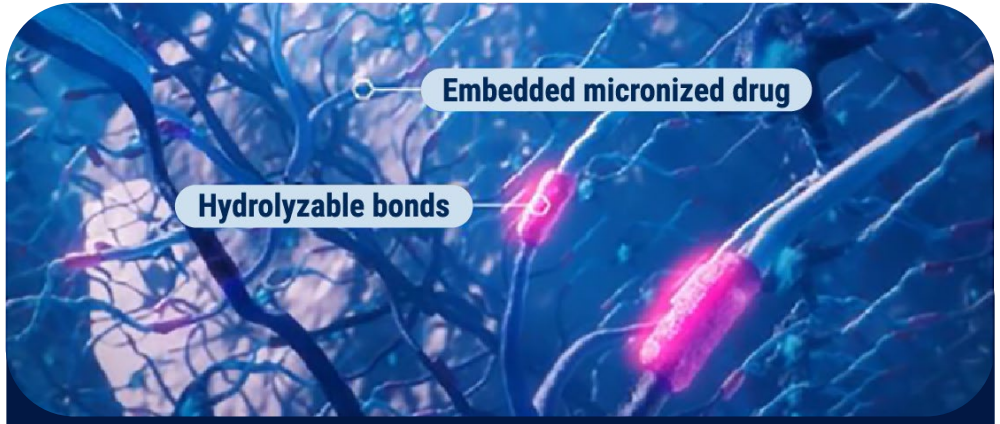


Highly selective pan VEGF inhibitor[1]
Highly potent TKI[2]

+

HYDROGEL TECHNOLOGY

Bioresorbable, Sustained Drug Delivery



Proprietary hydrogel
Versatile, biocompatible, tunable platform[3]

OTX-TKI

is being developed with the aim to provide:

- **A single hydrogel insert**[3,4]
- **Continuous and consistent delivery up to 12 months**[3,5]
- **Complete and predictable bioresorption**[3,5]

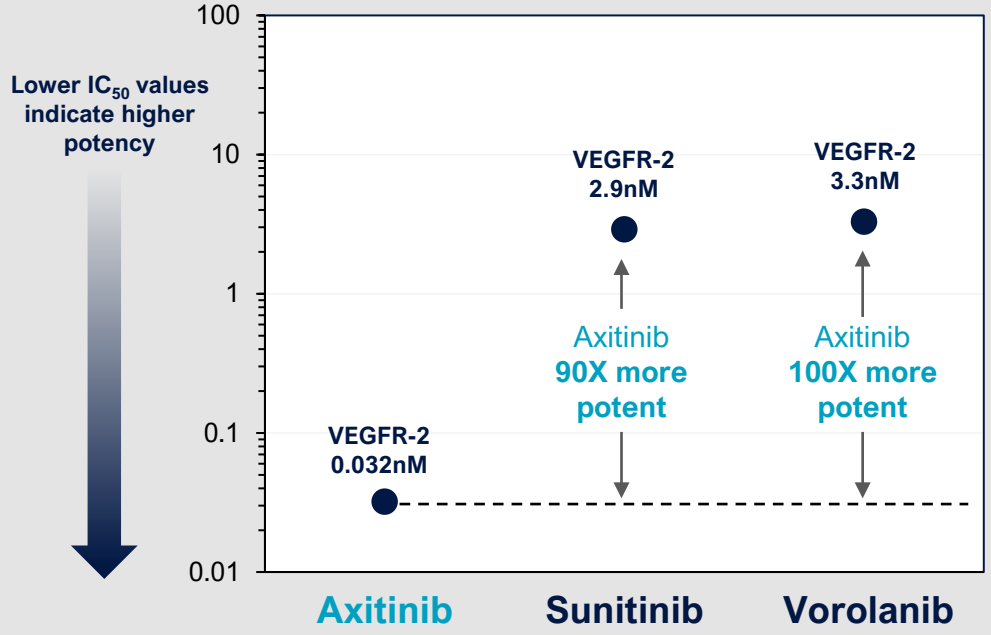
OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

1. Zhao Y, et al. *Oncologist.* 2015;20(6):660-673. 2. Gross-Goupil M, et al. *Clin Med Insights Oncol.* 2013;7:269-277. 3. Blizzard CD, et al. Ocular Implant Containing a Tyrosine Kinase Inhibitor. US Patent 11,439,592 B2. September 13, 2022. 4. Tan CS, et al. *Clin Ophthalmol*. 2022;16:917-933. 5. Data on File 033. Ocular Therapeutix. 2026.
TKI, Tyrosine Kinase Inhibitor; VEGF, Vascular Endothelial Growth Factor

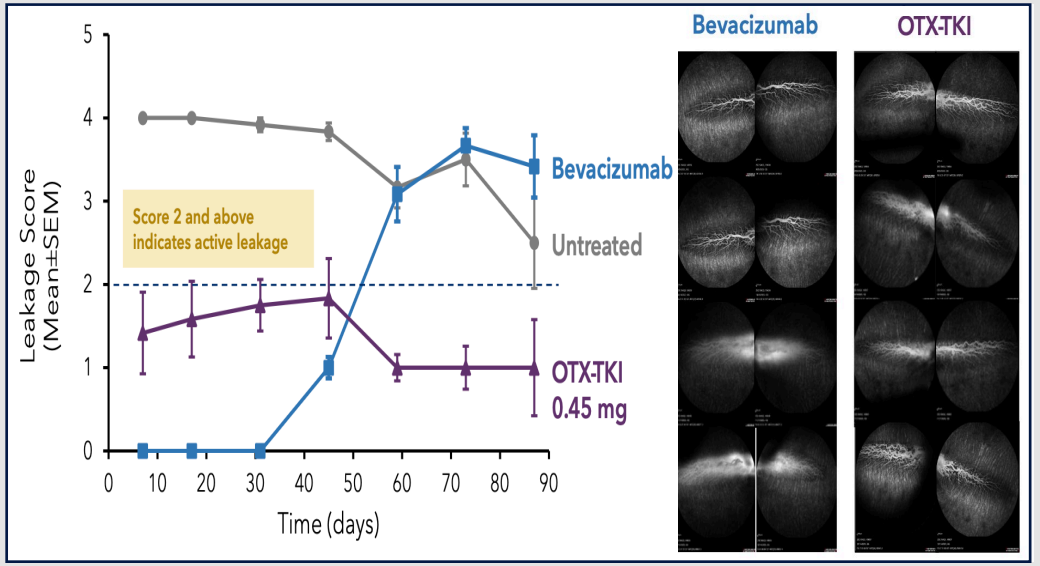
Axitinib: Highly Selective, Very Potent, pan-VEGFR Inhibitor

IC_{50} for VEGF Receptor 2 (nM)[1-3]



Highly selective for all VEGF receptors, ~100x more potent for VEGFR-2[1-3]

VEGF Challenge Rabbit Model[2]



Sustained leakage control in repeat VEGF challenge animal model[2]

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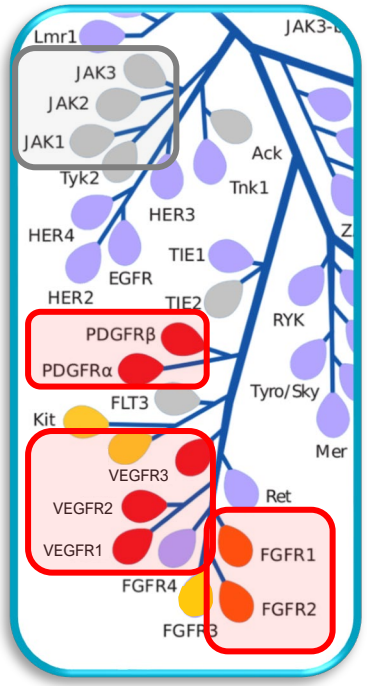
1. Patel C, et al. Target and Selectivity Profiling of Axitinib in Cell-Based and Biochemical Assays. Presented at Association in Vision and Ophthalmology. May 4, 2025. Salt Lake City, UT. **2.** Blizzard, C et al. Pharmacodynamic efficacy of optimized intravitreal axitinib implant (OTX-TKI) in a VEGF challenge rabbit model. Presented at the Association in Vision and Ophthalmology. May 9, 2024. Seattle, WA, US. **3.** Reaction Biology, Germany; Cellular Phosphorylation Assay Service. (https://www.reactionbiology.com) CHO Cellular assay data demonstrated no TIE2 inhibition within physiological drug solubility range at normal cellular ATP levels via the gold standard cell phosphorylation assay; Ocular Therapeutix. Data on File 042. 2026.

VEGFR, vascular endothelial growth factor receptor; IC50, inhibitory concentration 50%; SEM, standard error of mean

Axitinib demonstrates strongest inhibition of all VEGF/PDGF/FGF Receptors

AssayQuant (Fluorescence Assay)*

1μM Axitinib*



1 mM ATP | **Physiologic Testing Conditions**

1μM* | Axitinib intraocular conc = 1.03 to 1.13 μM; Vorolanib intraocular conc = 0.23 to 0.95 μM[3,4,6]

Kinase[1,2]	Axitinib	Vorolanib[3-5]	Sunitinib
VEGF RECEPTORS			
VEGFR1	99%	39%	83%
VEGFR2	97%	28%	71%
VEGFR3	95%	59%	72%
OTHER RECEPTORS			
PDGFRα	79%	42%	70%
PDGFRβ	88%	41%	87%
FGFR1	76%	0%	45%
FGFR2	76%	16%	54%
FGFR3	67%	15%	63%
JAK1	18%	13%	52%

Reaction Biology (Radiometric Assay)**

1 mM ATP | **Physiologic Testing Conditions**

1μM* | Axitinib intraocular conc = 1.03 to 1.13 μM; Vorolanib intraocular conc = 0.23 to 0.95 μM[3,4,6]

Kinase[1,2]	Axitinib	Vorolanib[3-5]	Sunitinib
VEGF RECEPTORS			
VEGFR1	72%	6%	12%
VEGFR2	76%	6%	14%
VEGFR3	63%	27%	18%
OTHER RECEPTORS			
PDGFRα	54%	37%	37%
PDGFRβ	79%	75%	76%
FGFR1	69%	12%	28%
FGFR2	62%	17%	28%
FGFR3	87%	40%	58%
JAK1	5%	14%	0%

Inhibition Key: <50% | 50-70% | 70-85% | 85-100% | Not tested

OCULAR THERAPEUTIX — Retina experience redefined™

*Kinome Tree inhibition analysis conducted in collaboration with AssayQuant. PhosphoSens® assay (AssayQuant®) conducted at 1mM ATP and 1μM drug concentrations. **Reaction Biology HotSpot kinase screening (Radiometric Assay) conducted at 1mM ATP and 1μM drug concentrations.

1. Data on file, Ocular Therapeutix. 2. Patel C, et al. Target and Selectivity Profiling of Axitinib in Cell-Based and Biochemical Assays. Presented at the Association for Research in Vision and Ophthalmology. May 8, 2025, Salt Lake City, UT. 3. Singh RP, et al. A 12-Month, Ocular Pharmacokinetic Study of EYP-1901, a Sustained-release, Intravitreal Formulation of the Tyrosine Kinase Inhibitor Vorolanib. Presented at the American Society of Retina Specialists Annual Meeting; July 28–August 1, 2023; Seattle, WA; 4. Kupperman BD, et al. Poster B0301. Presented at ARVO 2024 Annual Meeting, May 5–9, 2024; Seattle, WA; 5. Xiu X, et al. *Organic Process Research & Development*. 2024;28(2):492-499; 6. Saim, S., Howard-Sparks, M., Paggiarino, D., Karzoun, B. and Chen, J., Eyepoint Pharmaceuticals Inc, 2026. Bioerodible ocular drug delivery insert and therapeutic method. U.S. Patent 12,551,368.; TKI, tyrosine kinase inhibitor; ATP, adenosine triphosphate; VEGFR, vascular endothelial growth factor receptor; PDGFR, platelet-derived growth factor receptor; FGFR, fibroblast growth factor receptor; JAK, janus kinase. TIE2, tyrosine kinase with immunoglobulin-like and epidermal growth factor–like domains-2.

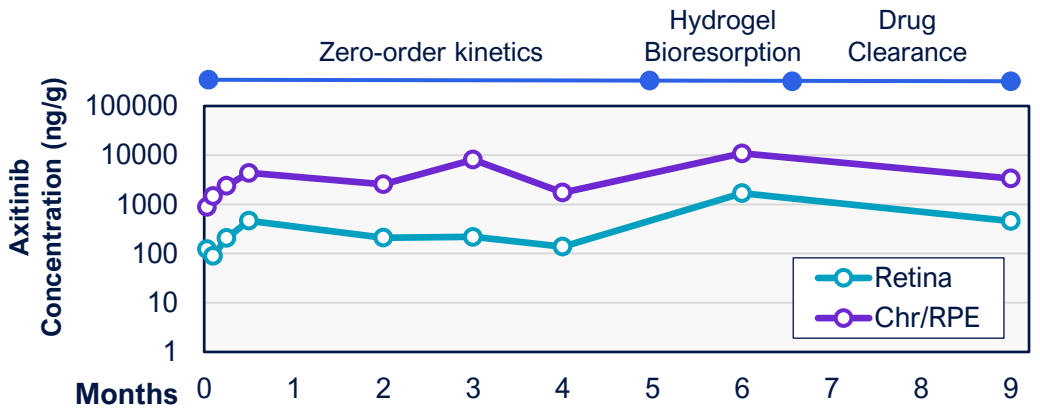
OTX-TKI is Designed to Release Axitinib and Maintain Intraocular Drug Levels Over Time

OTX-TKI In Vivo Delivery Profile[1]

Rapid, continuous and consistent axitinib delivery

Targeted drug delivery to retina and choroid

Axitinib concentrations following a single OTX-TKI in NHPs[1]



OCULAR THERAPEUTIX Retina experience redefined™

1. Data on File 033. Ocular Therapeutix. 2. Li J, et al. *Nat Rev Mater.* 2016;1(12):16071. 3. Müller DA, et al. *J Orthop Surg Res*. 2016;11(1):111.
Chr, choroid; RPE, retinal pigment epithelium; NHP, non-human primate.

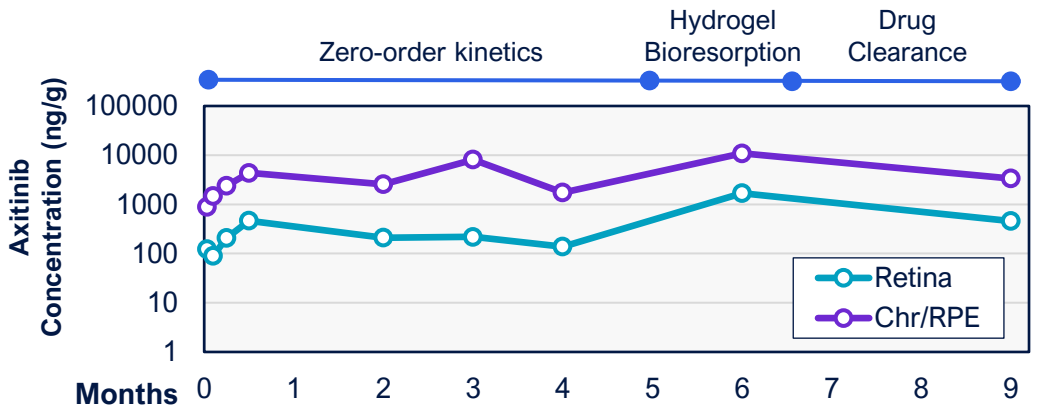
OTX-TKI is Designed to Release Axitinib and Maintain Intraocular Drug Levels Over Time with Complete Bioresorption

OTX-TKI In Vivo Delivery Profile[1]

Rapid, continuous and consistent axitinib delivery

Targeted drug delivery to retina and choroid

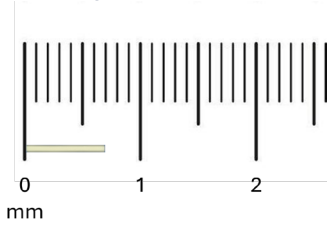
Axitinib concentrations following a single OTX-TKI in NHPs[1]

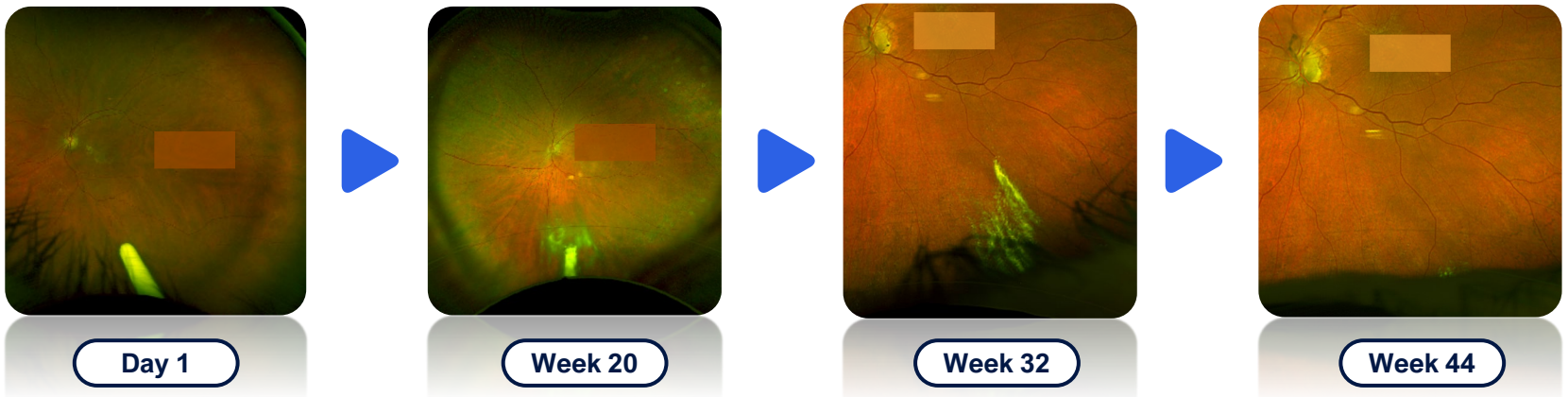


Hydrogel bioresorbs completely and predictably via hydrolysis for potential redosing[1-3]

Dry OTX-TKI Dimensions

7mm length, 0.4mm diameter





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1. Data on File 033. Ocular Therapeutix. 2. Li J, et al. *Nat Rev Mater.* 2016;1(12):16071. 3. Müller DA, et al. *J Orthop Surg Res*. 2016;11(1):111.
Chr, choroid; RPE, retinal pigment epithelium; NHP, non-human primate.

OTX-TKI is Designed for Seamless, Immediate Adoption

Ideal Target Product Profile

Pan-VEGF and PDGF inhibitory activity[1]

Axitinib has best-in-class (TKI) potency[1]

Extended durability up to 12 months[2]

Single Bioresorbable Hydrogel

No remnants[3]

Tunable hydrogel[4]

Hydrogel used in over 5 million patients[5]

Optimizing for Retina Practices

Familiar IVT injection with **25g needle**[6]

Predictable schedule for patients[2]

Designed for **improved treatment adherence**[2]

OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

1. Gross-Goupil M, et al. *Clin Med Insights Oncol*. 2013;7:269-277. 2. Eichenbaum, DA, et al. American Academy of Ophthalmology Annual Meeting; October 18-21, 2024; Chicago, IL. 3. Data on File 044. Ocular Therapeutix. 2026.. 4. Blizzard CD, et al. Ocular Implant Containing a Tyrosine Kinase Inhibitor. US Patent 11,439,592 B2. September 13, 2022. 5. Stuart M. Instylla: An easy, predictable, and simpler way to embolize tumors. MedTech Strategist. 2021.. 6. Almony A. *Am J Manag Care*. 2023;29(suppl 6):S81-S89 .
VEGF, vascular endothelial growth factor; PDGF, platelet-derived growth factor; IVT, intravitreal.

OTX-TKI Phase 3 Clinical Programs

Evaluating the efficacy, durability, and safety of OTX-TKI in nAMD

nAMD

SOL-1

Superiority Trial

Durability of a single OTX-TKI injection

SOL-R

Non-Inferiority Trial

Repeat dosing every 6 months

SOL-X

Open-Label Extension

Long-term safety and disease modifying potential of continuous VEGF suppression*

Complementary studies designed to provide a comprehensive characterization of OTX-TKI across patient populations

OCULAR THERAPEUTIX Retina experience redefined™

nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor
*Eligible patients who complete end of Year 2 visit in SOL-1 or SOL-R

OTX-TKI Phase 3 Clinical Programs

Evaluating the efficacy, durability, and safety of OTX-TKI in nAMD

nAMD

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OCULAR THERAPEUTIX Retina experience redefined™

nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor
*Eligible patients who complete end of Year 2 visit in SOL-1 or SOL-R

OTX-TKI Evaluated in a Superiority nAMD Trial Designed to Align with FDA Guidance

	FDA Guidance for nAMD Trials	SOL-1 Trial Design
Dosing Schedule	**One comparator arm should have the same dosing schedule** as the investigational drug[1]	**Both study arms have same dosing schedule**
Sham Injections	**Sham injections are not recommended;** considered inadequate masking[2,3]	**No sham injections**
Superiority Endpoint	**≥15-Letter**[1] **Decrease** OR **Increase** OR **Difference**	**≥15-Letter Decrease** Proportion with <15 ETDRS letters of BCVA loss from baseline at Week 36

SOL-1

- Compares a single OTX-TKI (0.45 mg) dose to a single aflibercept (2 mg) dose
- Designed to show superiority on efficacy and durability
- SOL-1 is being conducted under a **Special Protocol Assessment**

OCULAR THERAPEUTIX Retina experience redefined

ClinicalTrials.gov. identifier: NCT06223958

1. U.S. Food and Drug Administration. *Neovascular AMD: Developing Drugs for Treatment Guidance for Industry*. Updated February 2023. Accessed April 1, 2026. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/neovascular-age-related-macular-degeneration-developing-drugs-treatment. 2. Type C WRO [written response only] Aug 2024. **3.** Weiss J, Boyd B, Event: Q&A with FDA, at the American Academy of Ophthalmology Annual Meeting, October 20, 2024

BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; nAMD, neovascular age-related macular degeneration

Study Design: OTX-TKI and Aflibercept Direct Comparison

SOL-1

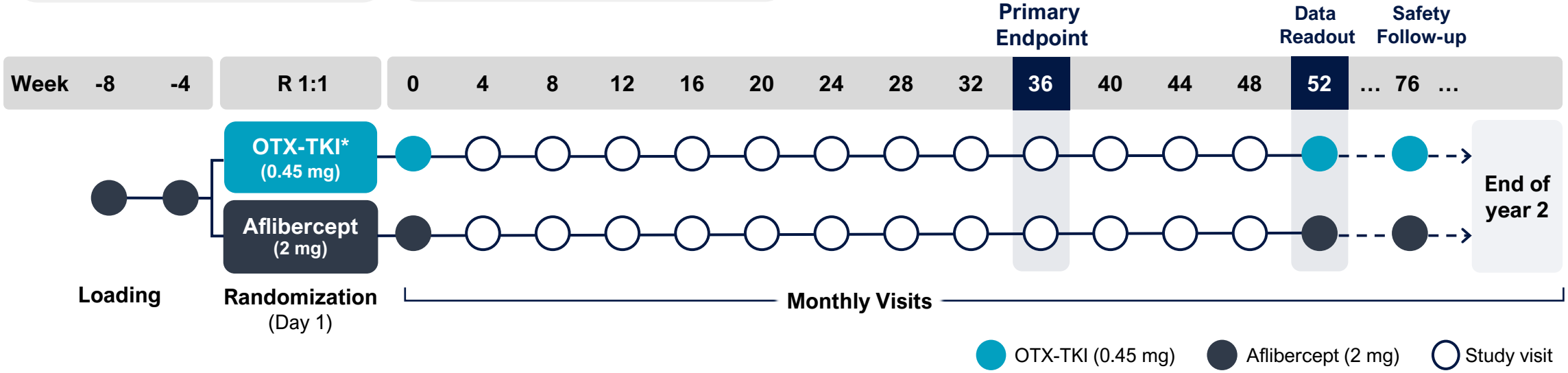
Key Enrollment Criteria (Screening)

- Treatment naïve for nAMD
- **BCVA ≥54 ETDRS letters** (~20/80)
- **CSFT of ≤500 µm**

Key Randomization Criteria (Day 1)

- **BCVA gain ≥10 ETDRS letters**
  OR
  BCVA ≥84 ETDRS letters (~20/20)
- **CSFT of ≤350 µm**

Proportion of subjects who maintained visual acuity, defined as <15 ETDRS letters of BCVA loss from baseline at Week 36



*No aflibercept injection is given at baseline; Two OTX-TKI subjects were misrandomized, did not receive study treatment and were not included in the full analysis set
ClinicalTrials.gov. identifier: NCT06223958
Rescue Criteria: BCVA loss ≥15 ETDRS letters from baseline due to nAMD; or New macular hemorrhage that would likely lead to irreversible vision loss if left untreated in the opinion of the investigator after discussion with Medical Monitor
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; nAMD, neovascular age-related macular degeneration; SD, standard deviation

Vision and Anatomic Improvement Observed After Two Aflibercept Injections

Baseline Characteristics

	Screening Visit *(Week −8)*		Baseline *(Randomization)*	
Study Eye Characteristics	**OTX-TKI 0.45 mg (N=172)**	**Aflibercept 2 mg (N=172)**	**OTX-TKI 0.45 mg (N=172)**	**Aflibercept 2 mg (N=172)**
BCVA, ETDRS letter score, mean (SD) Snellen Equivalent	70.9 (11.3) ~20/40	69.5 (10.8) ~20/40	80.8 (7.6) ~20/25	79.2 (7.9) ~20/25
CSFT, µm, mean (SD)	303.6 (72.5)	302.7 (78.3)	219.3 (37.1)	226.8 (42.1)

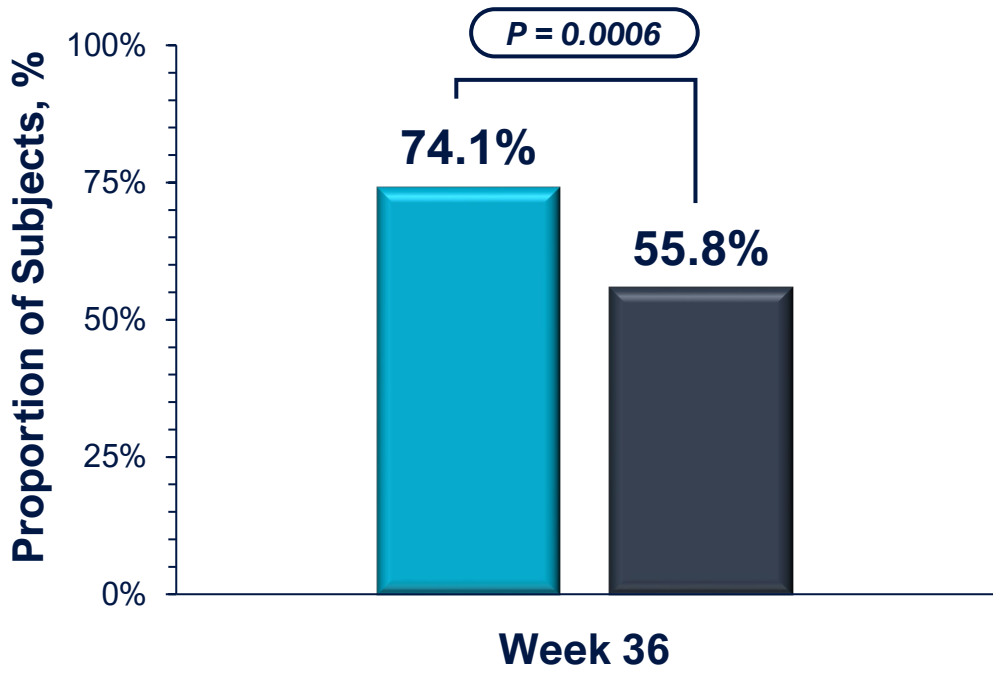
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study

Unmatched Durability: First Trial to Demonstrate Durability ≥9 Months

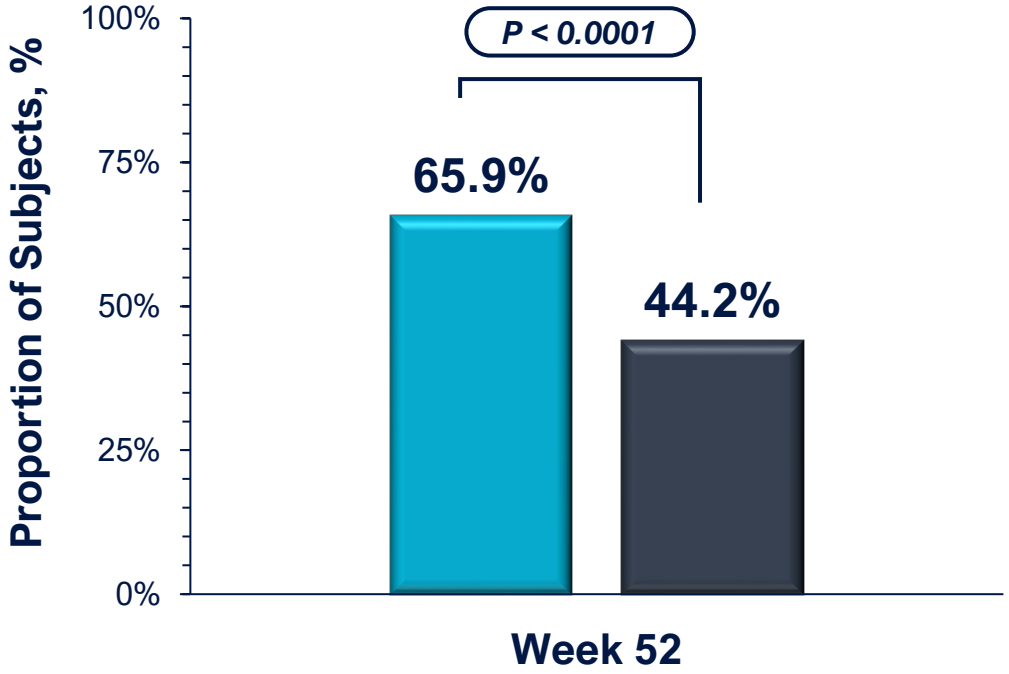
SOL-1

Maintenance of Visual Acuity*

Primary Endpoint



Key Secondary Endpoint



OTX-TKI 0.45 mg (n=170) Aflibercept 2 mg (n=172)

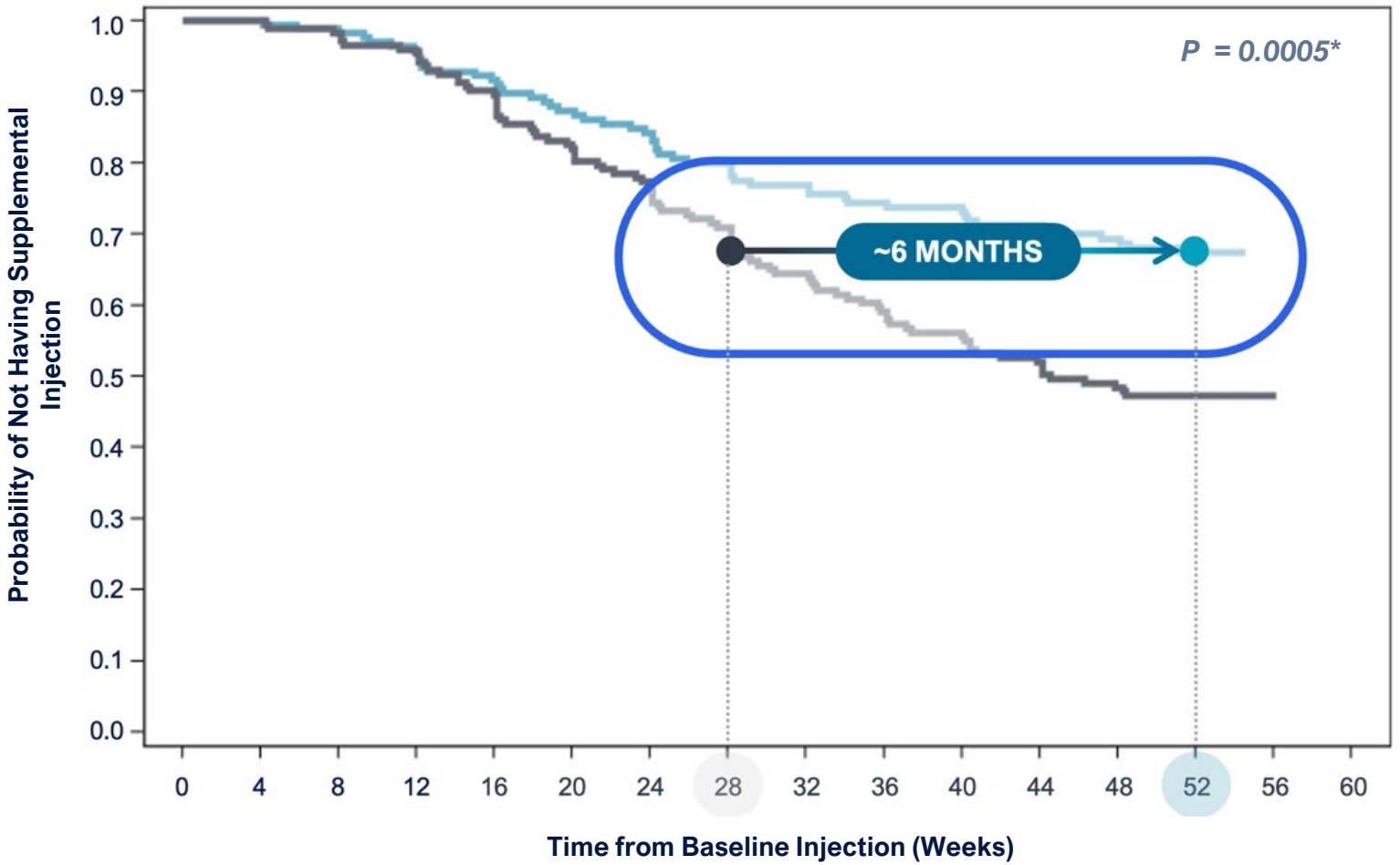
OCULAR THERAPEUTIX Retina experience redefined™

*Maintenance of vision defined as proportion of subjects who maintain visual acuity, a loss of <15 ETDRS letters of BCVA from baseline.
Predefined statistical rules were applied to adjust for treatment discontinuation or deviation as per the pre-specified statistical analysis plan. Full analysis set
Moshfeghi D. Presented at the American Academy of Ophthalmology Retina Subspecialty Day. October 9, 2026. New Orleans, LA
BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; SD, standard deviation

Significantly Lower Risk of Supplemental Treatments with OTX-TKI

SOL-1

Secondary Endpoint: Time to First Supplemental Treatment



~6 Month Difference

OTX-TKI Week 52 supplement-free rate reflects ***~6-month*** **advantage** over aflibercept

OTX-TKI 0.45 mg (n=170)
Aflibercept 2 mg (n=172)

OCULAR THERAPEUTIX Retina experience redefined™

Supplemental-free subjects include those who did not require rescue injections as specified by the protocol.
*Nominal P value

Sustained Disease Control: Visual and Anatomic Stability with OTX-TKI

SOL-1

Mean Change in BCVA and CSFT from Screening

Post Hoc Analysis

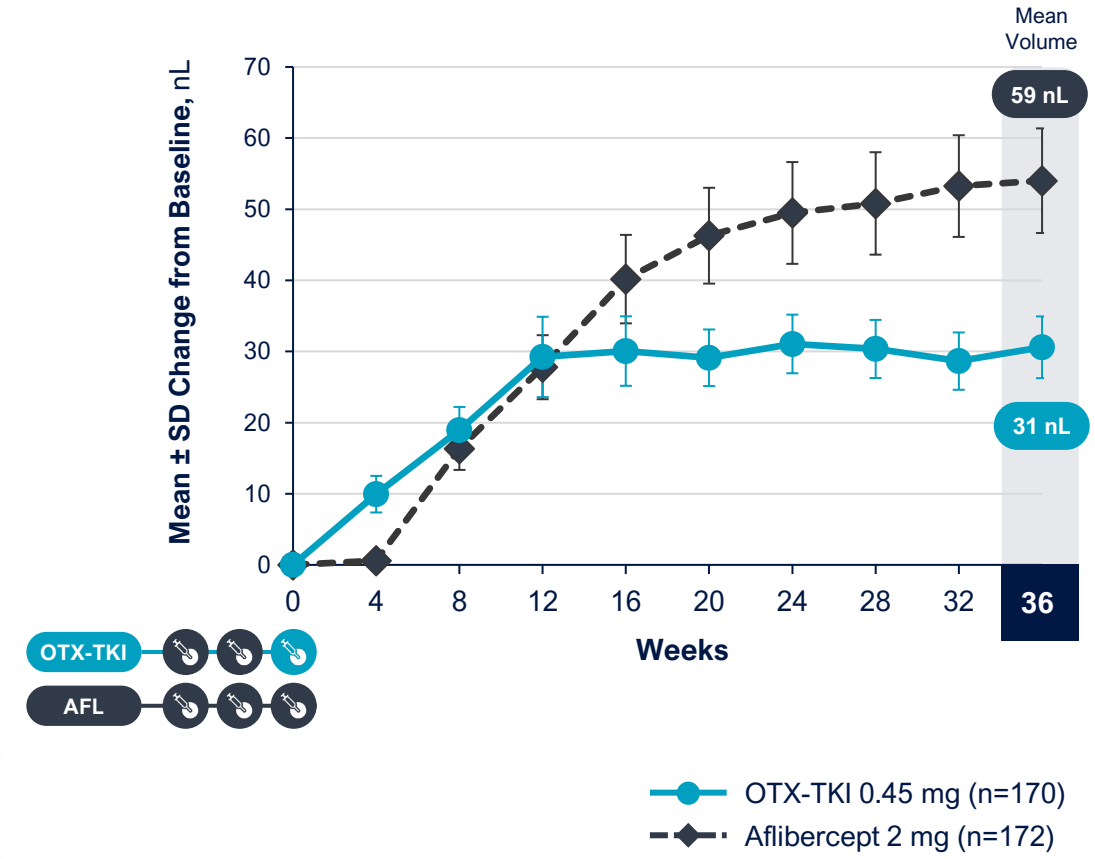


74.7% Supplemental free

56.4% Supplemental free

Mean Change in Retinal Fluid Volume

Prespecified Exploratory Endpoint



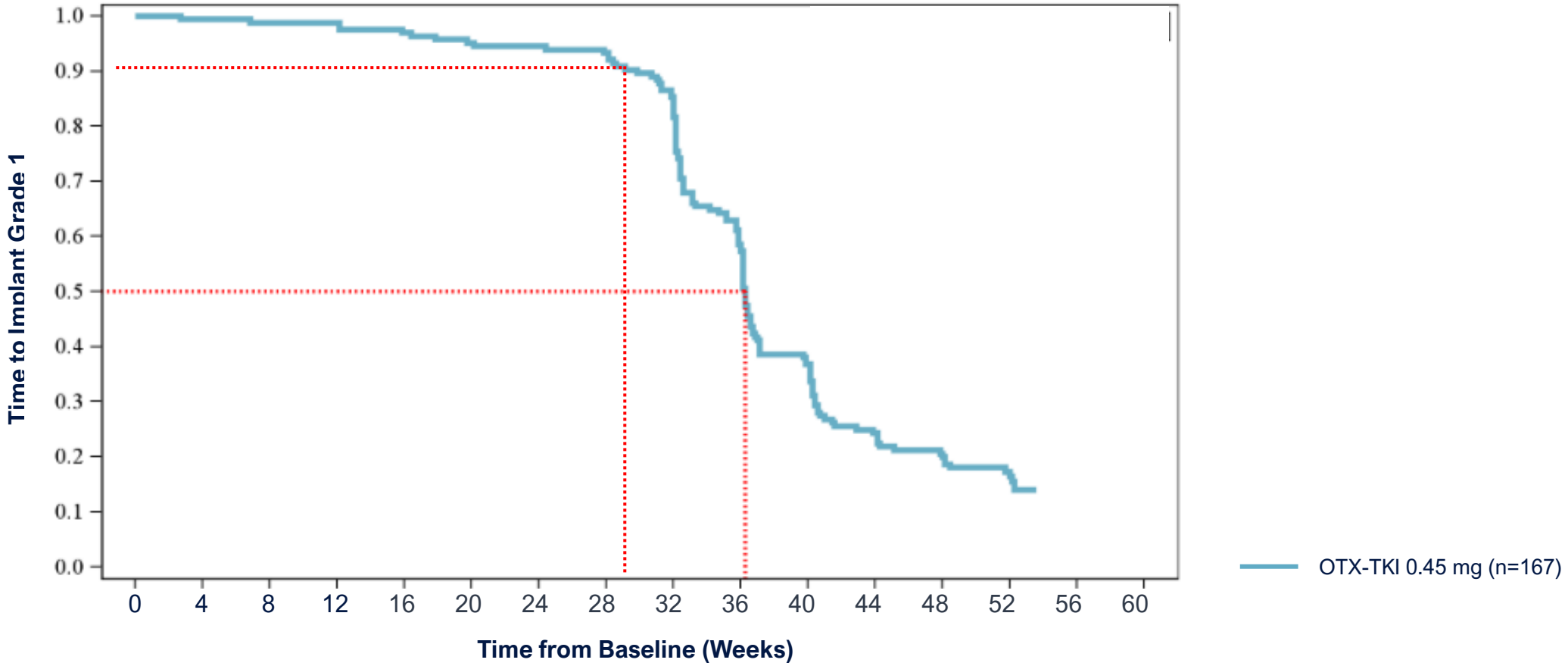
OCULAR THERAPEUTIX Retina experience redefined™

Full analysis set. For subjects who received any supplemental injections, their observed BCVA and CSFT values after the 1st supplemental injection are set to missing. Baseline measurements are the last non-missing measurement prior to the study drug injection on Day 1. Supplemental-free subjects include those who did not require rescue injections as specified by the protocol.
AFL, aflibercept; BCVA, best-corrected visual acuity; CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; ETDRS, Early Treatment Diabetic Retinopathy Study; IRF, intraretinal fluid; SRF, subretinal fluid; SE, standard error; SD, standard deviation

Intact OTX-TKI Implant Was Visible in >90% of Patients Beyond Month 6 and ~50% at Month 9

SOL-1

Post Hoc Analysis: Time to Hydrogel Dissipation



Axitinib release is sustained throughout the period of hydrogel persistence

Residual drug particles continue to provide therapeutic effects for several weeks

OCULAR THERAPEUTIX Retina experience redefined™

Kaplan–Meier analysis of time from Day 1 administration to the first Grade 1 implant assessment. Implant status was evaluated at scheduled study visits. Grade 3 indicates that the hydrogel implant remained fully intact, with the drug contained within the implant; Grade 2 indicates that the hydrogel implant had partially dissipated; and Grade 1 indicates that the hydrogel had fully dissipated, with released drug particles visible outside the implant in a localized or dispersed pattern.

Moshfeghi D. Presented at the American Academy of Ophthalmology Retina Subspecialty Day. October 9, 2026. New Orleans, LA

OTX-TKI was Generally Well Tolerated

SOL-1

Subjects with Ocular AEs in the Study Eye (>2%) Through Week 52, n (%)	OTX-TKI 0.45 mg n = 170	Aflibercept 2 mg n = 172
Vitreous floaters	21 (12.4)	2 (1.2)
Cataract	12 (7.1)	5 (2.9)
Conjunctival hemorrhage	11 (6.5)	5 (2.9)
Retinal hemorrhage	10 (5.9)	17 (9.9)
Dry eye	7 (4.1)	2 (1.2)
Vitreous detachment	7 (4.1)	3 (1.7)
Punctate keratitis	6 (3.5)	0
Vitreous opacities	6 (3.5)	0
Eye pain	5 (2.9)	1 (0.6)
Anterior chamber opacity	4 (2.4)	0
Posterior capsule opacification	4 (2.4)	6 (3.5)

Intraocular Inflammation

- Nine events observed in study eyes of 7 subjects in the OTX-TKI arm
  - All cases were mild or moderate in severity and resolved
- **There were no cases of endophthalmitis, occlusive or non-occlusive retinal vasculitis**

AE, adverse event; IOI, intraocular inflammation

Appearance of Floaters May Correspond to Hydrogel Dissolution and Drug Elution

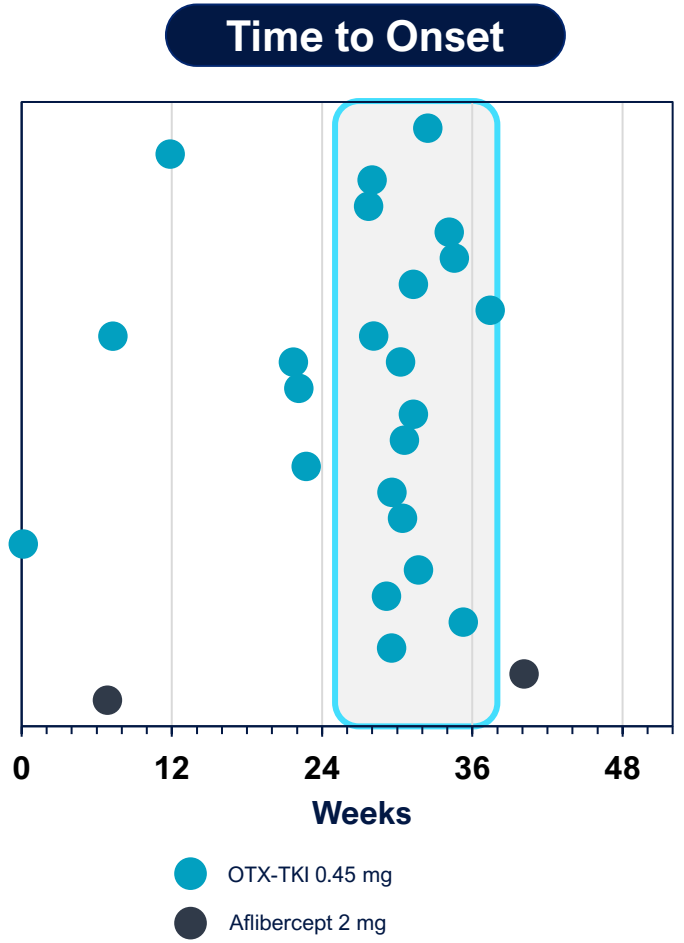
SOL-1

Evaluation of Vitreous Floaters



	OTX-TKI 0.45 mg n = 23*	Aflibercept 2 mg n = 2
Time to onset, days		
Mean (SD)	187.9 (64.0)	164.5 (164.8)
Median	207.0	164.5
BCVA change from prior visit before onset of floaters, ETDRS letters		
Mean change (SD)	-0.4 (5.0)	-5.5 (6.4)
Median change	0.0	-5.5

- All cases were mild to moderate in severity
- No evidence of IOI associated with floaters
- Onset of vitreous floaters AE coincides with drug elution stage of OTX-TKI hydrogel bioresorption process
- **For all subjects** with vitreous floaters AE reported, **drug particles are no longer visible**



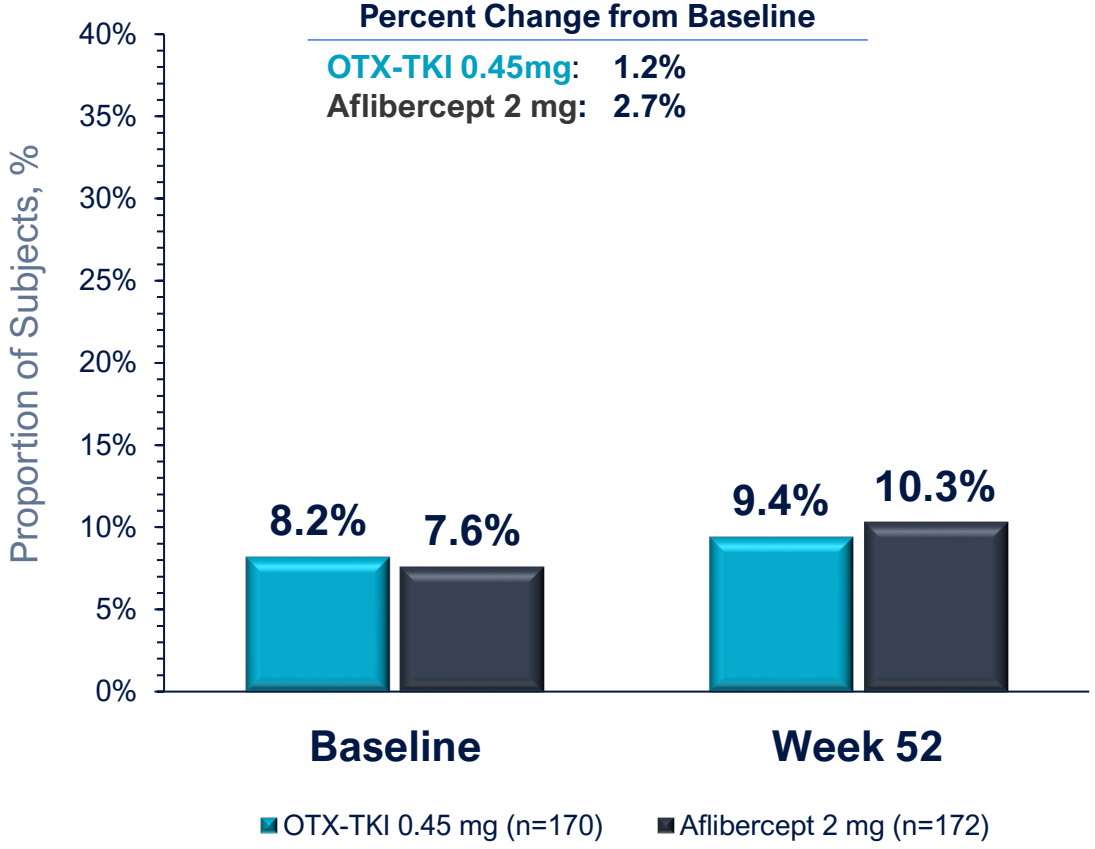
OCULAR THERAPEUTIX Retina experience redefined™

*23 events in the study eye, 21 subjects; No case observed to be associated with cataract formation
Optos images on day of onset of AE of vitreous floaters
OTK-TKI: Mean change from baseline (SD) in BCVA, -3.3 (8.2) ETDRS letters; median change from baseline, -1.0 ETDRS letters
Study is ongoing until Year 2
SD, standard deviation; BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; AE, adverse events; IOI, intraocular inflammation

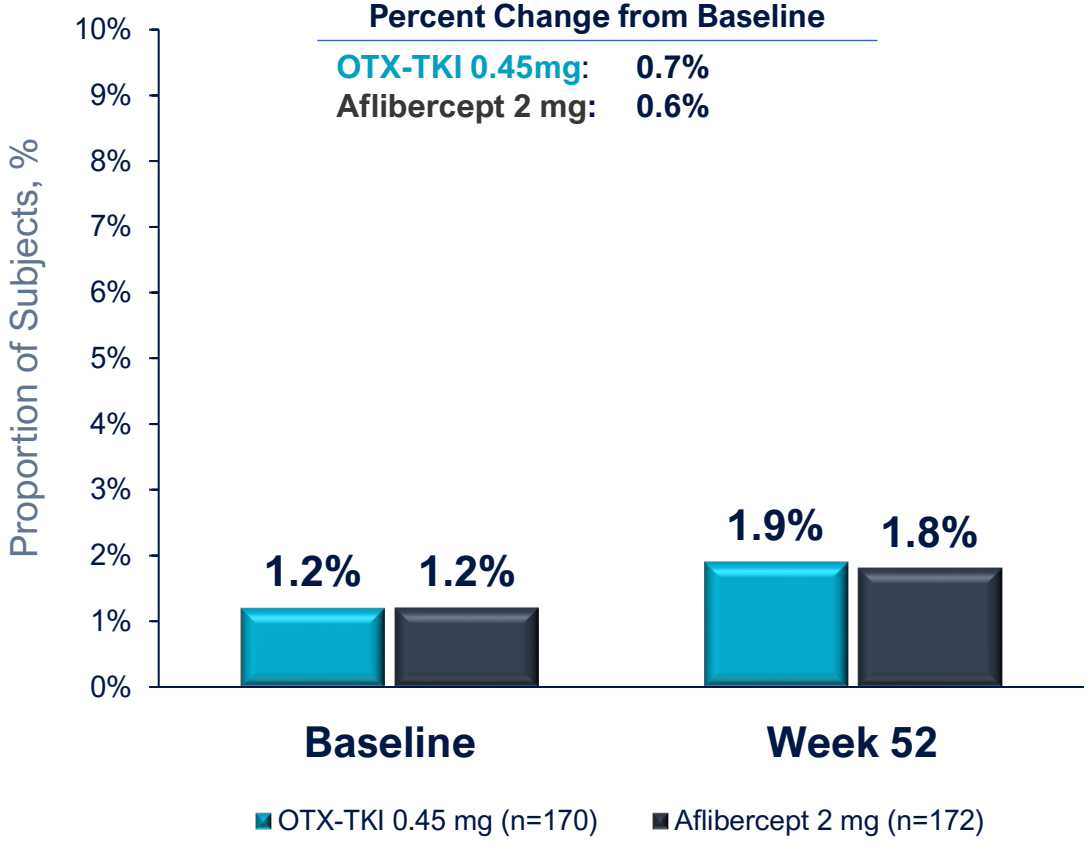
Incidence of Macular Atrophy in SOL-1

Safety Analysis

Any Macular Atrophy[1]



Macular Atrophy in the Central 1mm[1]



[1]cRORA measured by the reading center

cRORA, complete retinal pigment epithelium and outer retinal atrophy

SOL-1 Results Demonstrate Potential Treatment Benefit of OTX-TKI

SOL-1

Superiority Primary Endpoint Successfully Met

OTX-TKI Demonstrated Superior Maintenance of Vision Compared to Aflibercept 2mg at Week 36*

First trial to demonstrate durability ≥ 9 months

In a post hoc analysis, 74.7% of subjects treated with OTX-TKI did not receive supplemental treatments by Week 36

Unmatched Durability

Visual and anatomic stability with OTX-TKI

In a post hoc analysis, OTX-TKI subjects maintained visual and anatomical outcomes, with most remaining supplement-free through Week 36

Sustained Disease Control

OTX-TKI demonstrated a well-tolerated safety profile through Week 52

There were no cases of endophthalmitis, occlusive or non-occlusive retinal vasculitis

Well-Tolerated

OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

*Maintenance of vision defined as proportion of subjects who maintain visual acuity, a loss of <15 ETDRS letters of BCVA from baseline
Supplemental-free subjects include those who did not require rescue injections as specified by the protocol

SOL-1: Insights Into Treatment Response

Yasha S. Modi MD, MHS



OCULAR THERAPEUTIX Retina experience redefined

Key Questions Emerging from the Data

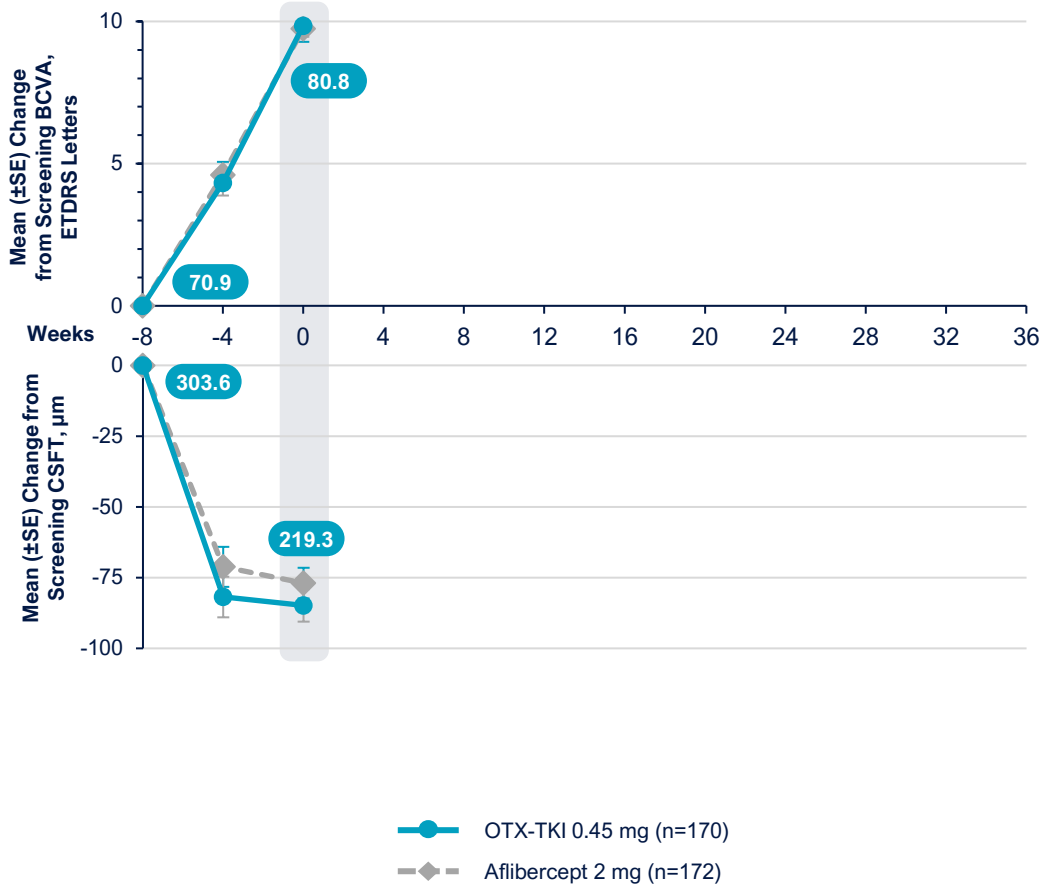
SOL-1

In patients similar to those enrolled in SOL-1, what outcomes and injection burden are observed with routine anti-VEGF care?

How may early fluid control with OTX-TKI inform treatment decisions in clinical practice?

How Does SOL-1 Data Align with Real World Outcomes?

SOL-1 Clinical Trial
Post Hoc Analysis



SOL-1 Emulated Population
IRIS Registry



Subjects (N=6178)

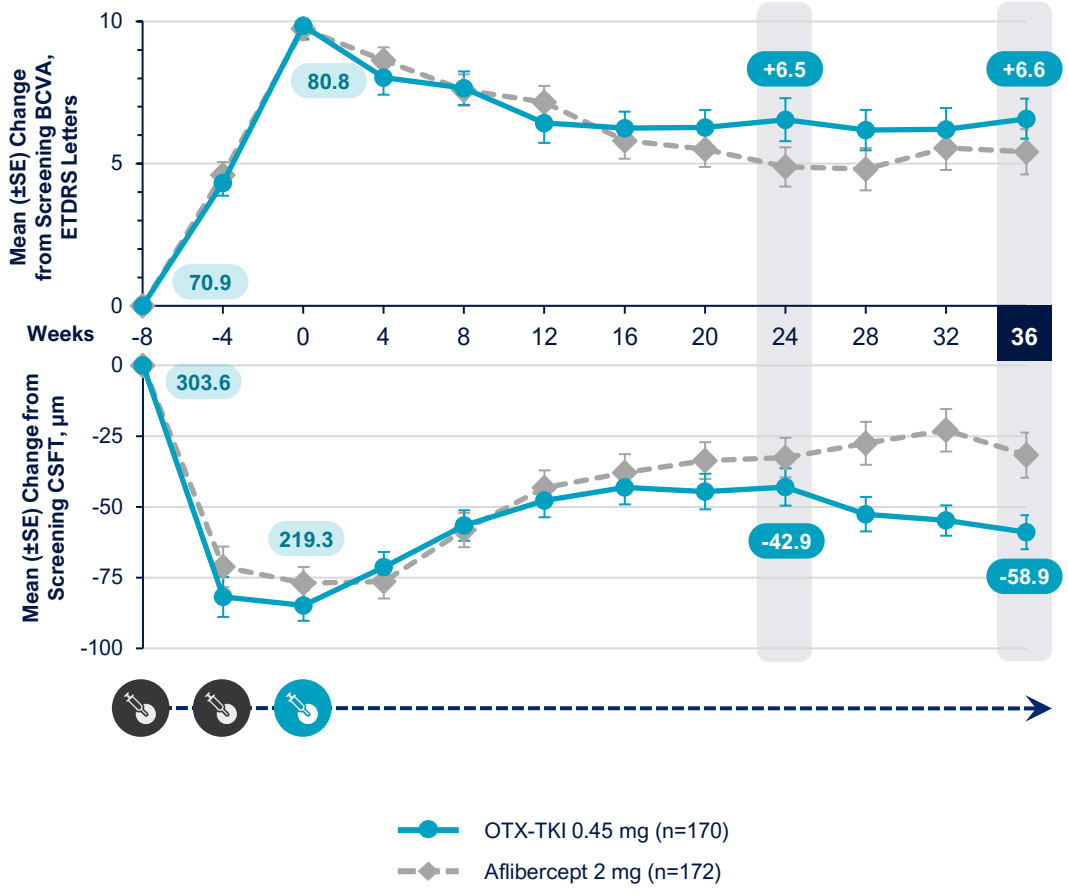
OCULAR THERAPEUTIX Retina experience redefined

AAO IRIS® Registry data were used to create a SOL-1–emulated population in a retrospective observational analysis applying SOL-1 eligibility and screening-response criteria. Outcomes through Week 36 are shown. Comparisons with SOL-1 are descriptive and nonrandomized.

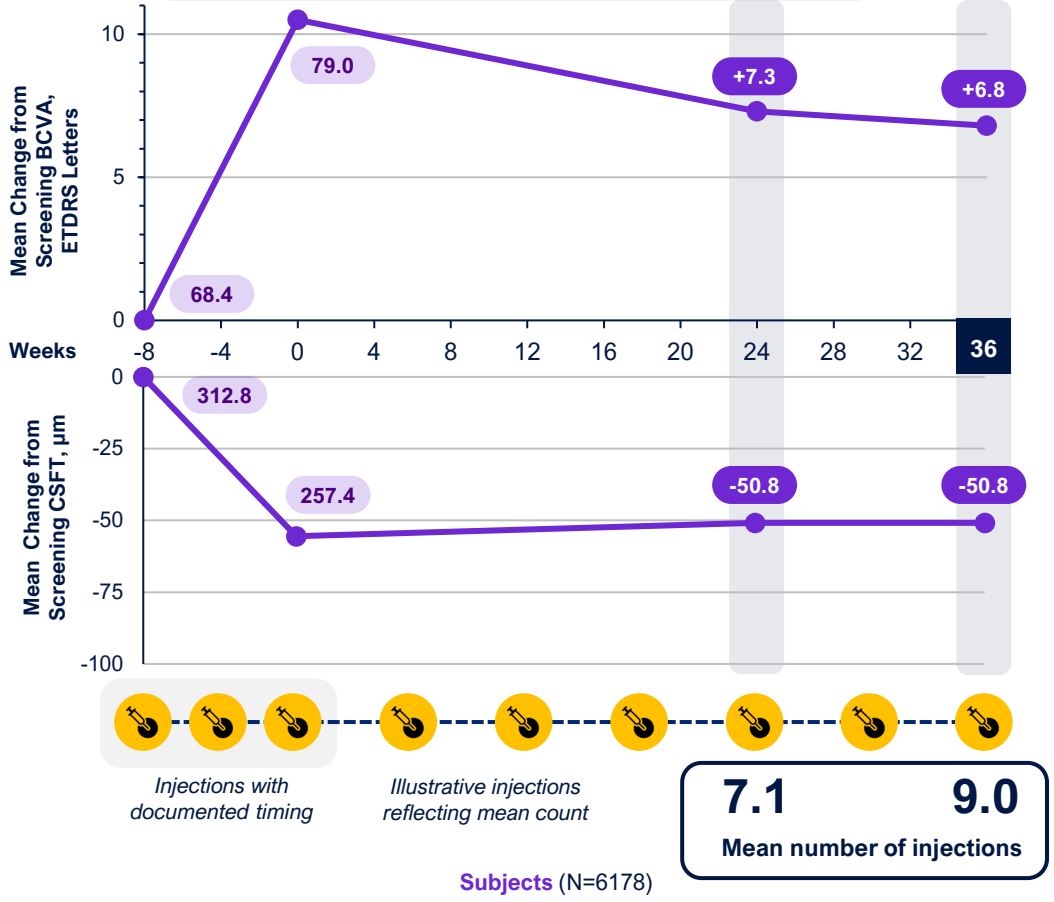
1. Data on file 046. Ocular Therapeutix; 2026.

How Does SOL-1 Data Align with Real World Outcomes?

SOL-1 Clinical Trial
Post Hoc Analysis



SOL-1 Emulated Population
IRIS Registry



AAO IRIS® Registry data were used to create a SOL-1–emulated population in a retrospective observational analysis applying SOL-1 eligibility and screening-response criteria. Outcomes through Week 36 are shown. Comparisons with SOL-1 are descriptive and nonrandomized.

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OCULAR THERAPEUTIX Retina experience redefined

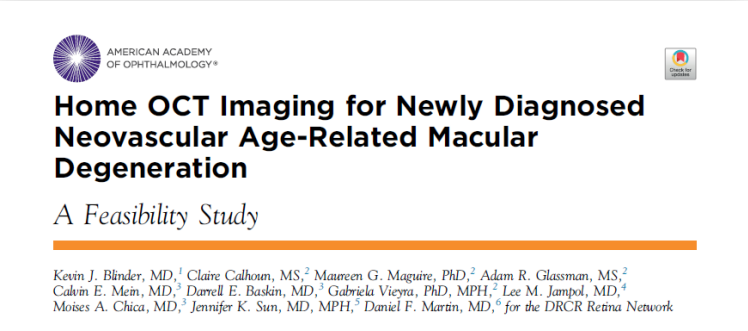
Key Questions Emerging from the Data

SOL-1

? *In patients similar to those enrolled in SOL-1, what outcomes and injection burden are observed with routine anti-VEGF care?*

? ***How may early fluid control with OTX-TKI inform treatment decisions in clinical practice?***

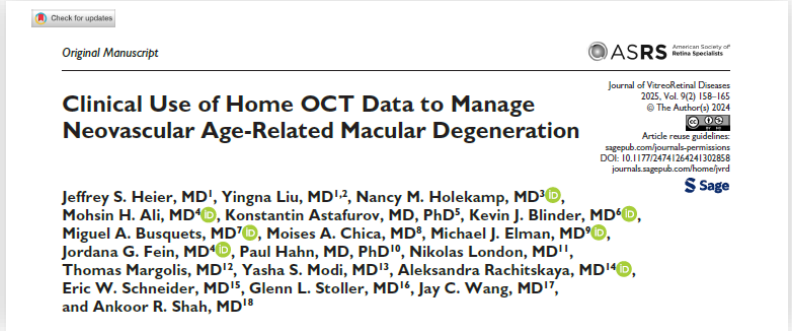
Real-World Retreatment Criteria and Quantitative Dryness Using AI-based Retinal Fluid Analysis


AMERICAN ACADEMY OF OPHTHALMOLOGY®

Home OCT Imaging for Newly Diagnosed Neovascular Age-Related Macular Degeneration

A Feasibility Study

Kevin J. Blinder, MD,[1] Claire Calhoun, MS,[2] Maureen G. Maguire, PhD,[2] Adam R. Glassman, MS,[2] Calvin E. Mein, MD,[3] Darrell E. Baskin, MD,[3] Gabriela Vieyra, PhD, MPH,[2] Lee M. Jampol, MD,[4] Moises A. Chica, MD,[3] Jennifer K. Sun, MD, MPH,[5] Daniel F. Martin, MD,[6] for the DRCR Retina Network


Check for updates

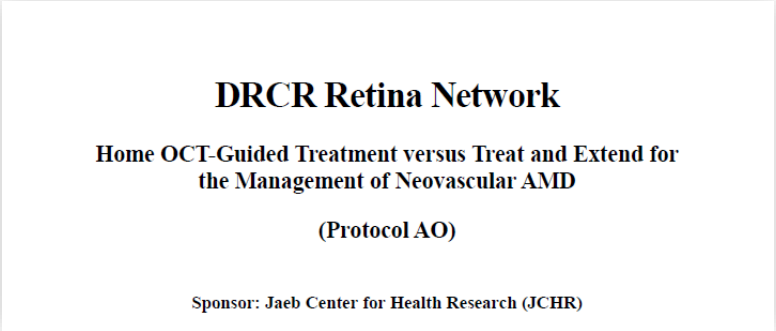
Original Manuscript

ASRS American Society of Retina Specialists

Clinical Use of Home OCT Data to Manage Neovascular Age-Related Macular Degeneration

Journal of VitreoRetinal Diseases
2025, Vol. 9(2) 158-165
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Sage

Jeffrey S. Heier, MD[1], Yingna Liu, MD[1,2], Nancy M. Holekamp, MD[3], Mohsin H. Ali, MD[4], Konstantin Astafurov, MD, PhD[5], Kevin J. Blinder, MD[6], Miguel A. Busquets, MD[7], Moises A. Chica, MD[8], Michael J. Elman, MD[9], Jordana G. Fein, MD[4], Paul Hahn, MD, PhD[10], Nikolas London, MD[11], Thomas Margolis, MD[12], Yasha S. Modi, MD[13], Aleksandra Rachitskaya, MD[14], Eric W. Schneider, MD[15], Glenn L. Stoller, MD[16], Jay C. Wang, MD[17], and Ankoor R. Shah, MD[18]


DRCR Retina Network

Home OCT-Guided Treatment versus Treat and Extend for the Management of Neovascular AMD

(Protocol AO)

Sponsor: Jaeb Center for Health Research (JCHR)

Defines Quantitative Dryness

≤10 nL of total retinal fluid was used as the definition of a dry retina[1]

Clinically Relevant

10 nL was the median total retinal fluid notification threshold selected by 15 retina specialists[2]

Implemented Prospectively

DRCR Protocol AO uses 10 nL as the total retinal fluid threshold that triggers an office visit[3]

Quantitative dryness defined as total IRF + SRF ≤10 nL

OCULAR THERAPEUTIX Retina experience redefined

Home OCT imaging used a 3 × 3 mm field.[1-3] In the SOL-1 analysis, quantitative dryness was defined as total IRF + SRF ≤10 nL within a 6 × 6 mm OCT analysis area.

1. Blinder KJ, et al. *Ophthalmol Retina.* 2024;8(4):376-387. 2. Heier JS, et al. *J Vitreoretin Dis.* 2025;9(2):158-165. 3. DRCR Retina Network. *Home OCT-Guided Treatment versus Treat and Extend for the Management of Neovascular AMD (Protocol AO).* Version 4.0. Jaeb Center for Health Research; March 21, 2025.

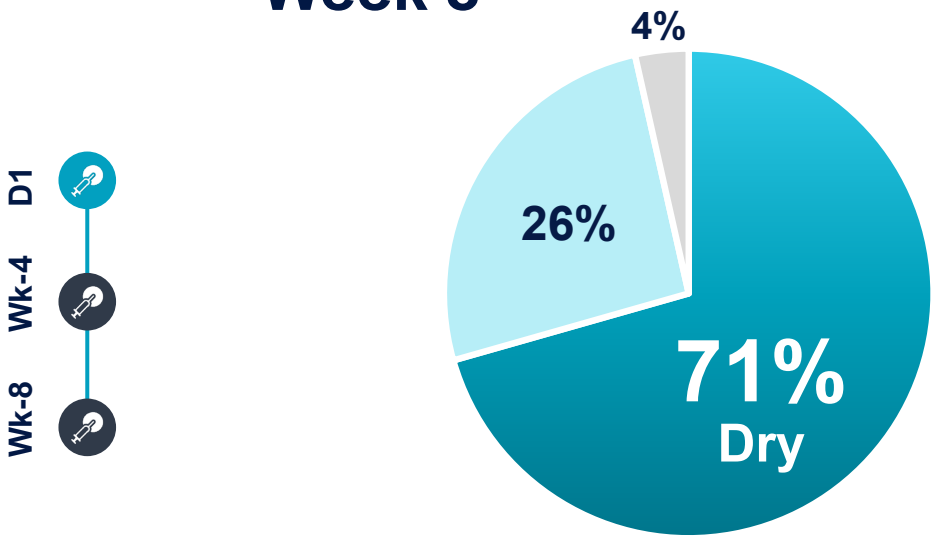
IRF, intraretinal fluid; SRF, subretinal fluid; OCT, optical coherence tomography; DRCR, Diabetic Retinopathy Clinical Research; AI, artificial intelligence; nL, nanoliters.

Most Patients in SOL-1 were Dry 8 weeks after Randomization with AI-based Retinal Fluid Analysis

Post Hoc Analysis: Quantitative Dry Retina Status at Week 8

OTX-TKI 0.45 mg (N=170)

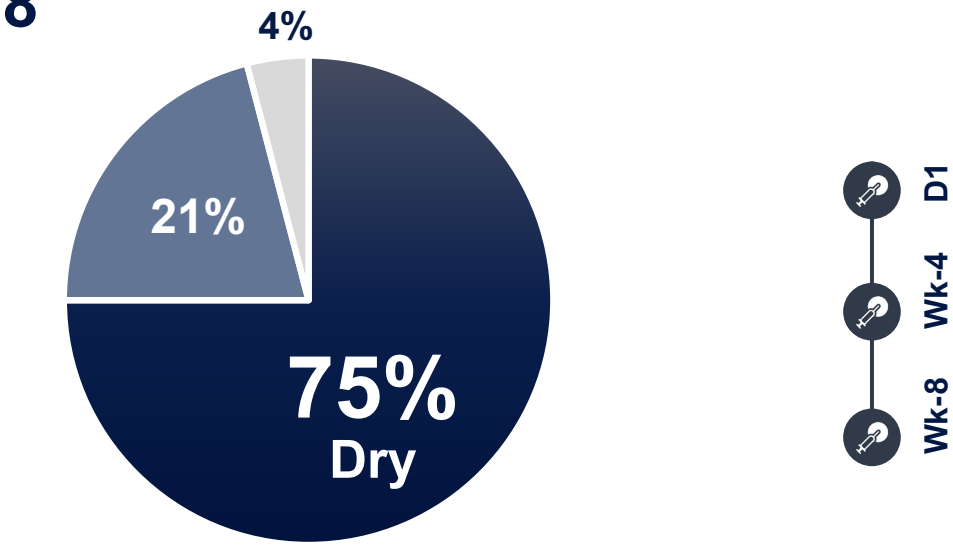
Week 8



- ≤10 nL increase (n = 120)
- >10 nL increase (n = 44)
- Missing (n = 6)

Aflibercept 2mg (N=172)

Week 8



- ≤10 nL increase (n = 129)
- >10 nL increase (n = 36)
- Missing (n = 7)

OCULAR THERAPEUTIX Retina experience redefined

Quantitative dryness defined as total intraretinal fluid and subretinal fluid volume ≤10 nL on AI-based OCT evaluation with manual grader correction of retinal fluid performed at Boston Image Reading Center (BIRC)
Moshfeghi D. Presented at the American Academy of Ophthalmology Retina Subspecialty Day. October 9, 2026. New Orleans, LA
Wk, week; D, day; nL, nanoliter; AI, artificial intelligence

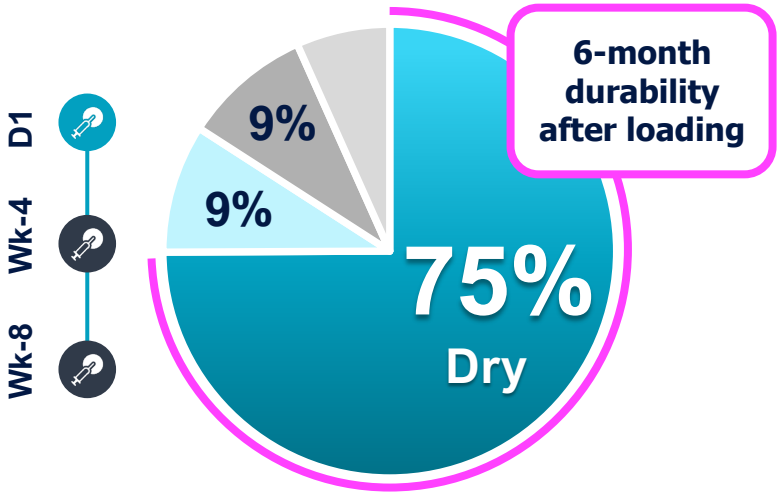
Using Real-World AI-based Retreatment Criteria, ~75% of OTX-TKI Patients Would Achieve 6-month Dosing*

SOL-1

Post Hoc Analysis: Subgroup of patients with Quantitative Dry Retina at Week 8

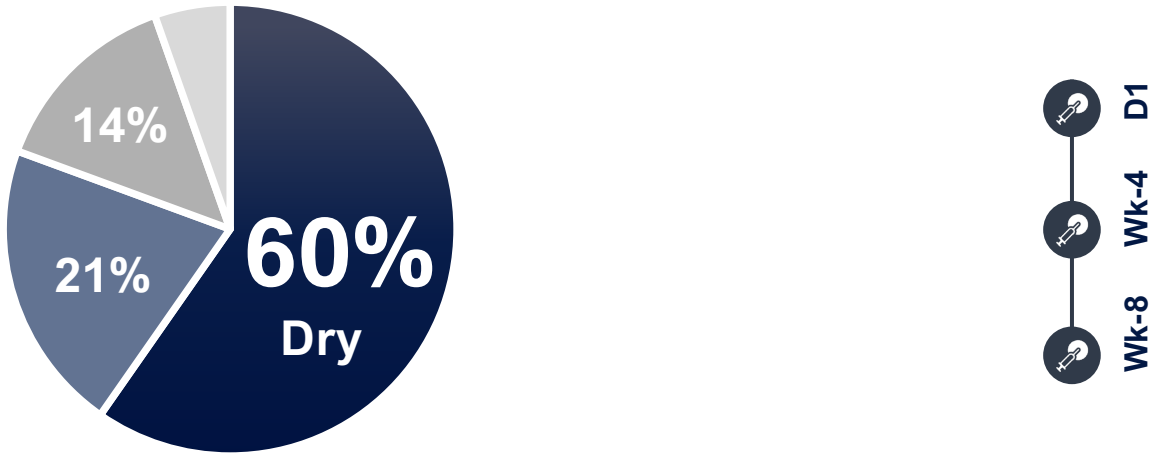
OTX-TKI 0.45 mg (n=120)

Week 24



Aflibercept 2mg (n=129)

Week 24



≤10nL increase
>10nL increase
Received supplemental treatment
Missing data

≤10nL increase
>10nL increase
Received supplemental treatment
Missing data

OCULAR THERAPEUTIX Retina experience redefined

*Approximately 75% of OTX-TKI–treated patients who were dry at Week 8 would achieve a 6-month dosing interval.
Quantitative dryness defined as total intraretinal fluid and subretinal fluid volume ≤10 nL on AI-based OCT evaluation with manual grader correction of retinal fluid performed at Boston Image Reading Center (BIRC). Analyses were based on observed cases. . For subjects who received supplemental treatment on or before Week 36, total retinal fluid measurements obtained after the first supplemental injection were treated as missing. Supplemental-free subjects include those who did not require rescue injections as specified by the protocol.
Wk, week; D, day; nL, nanoliter; AI, artificial intelligence

Using Real-World AI-based Retreatment Criteria, ~70% of OTX-TKI Patients Would Achieve 9-month Dosing*

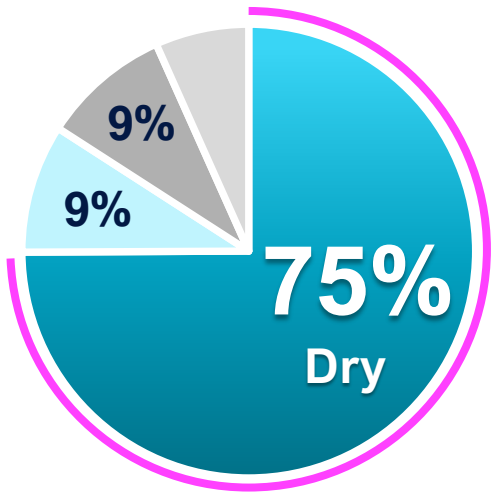
Post Hoc Analysis: Subgroup of patients with Quantitative Dry Retina at Week 8

SOL-1

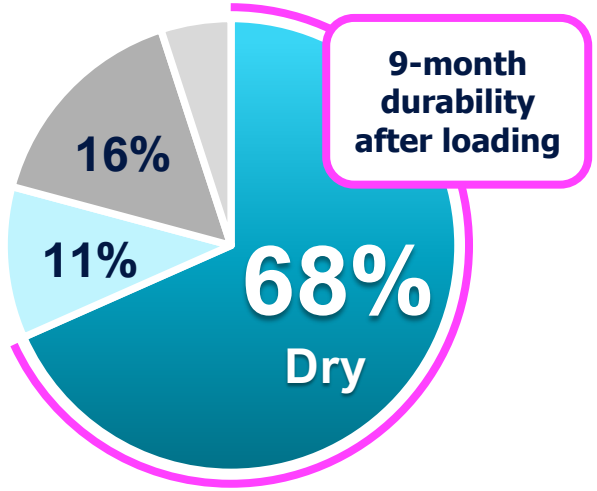
OTX-TKI 0.45 mg (n=120)

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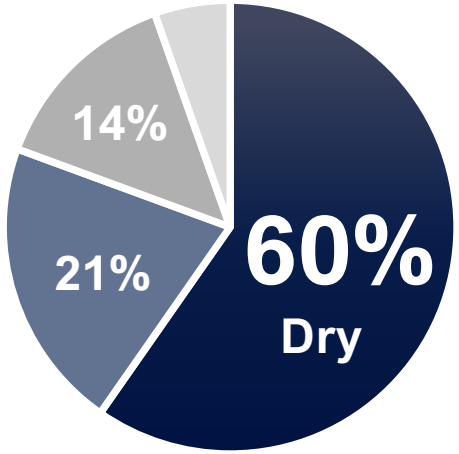
Week 24



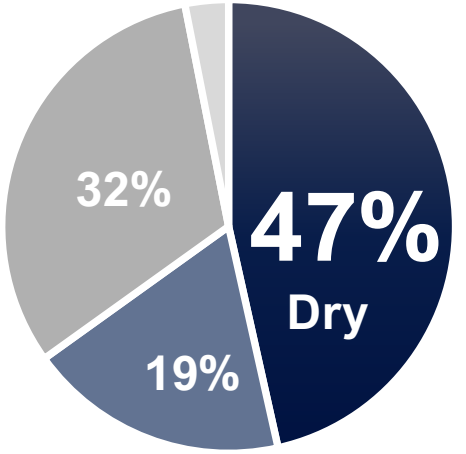
Week 36



Week 24



Week 36







≤10nL increase
>10nL increase
Received supplemental treatment
Missing data

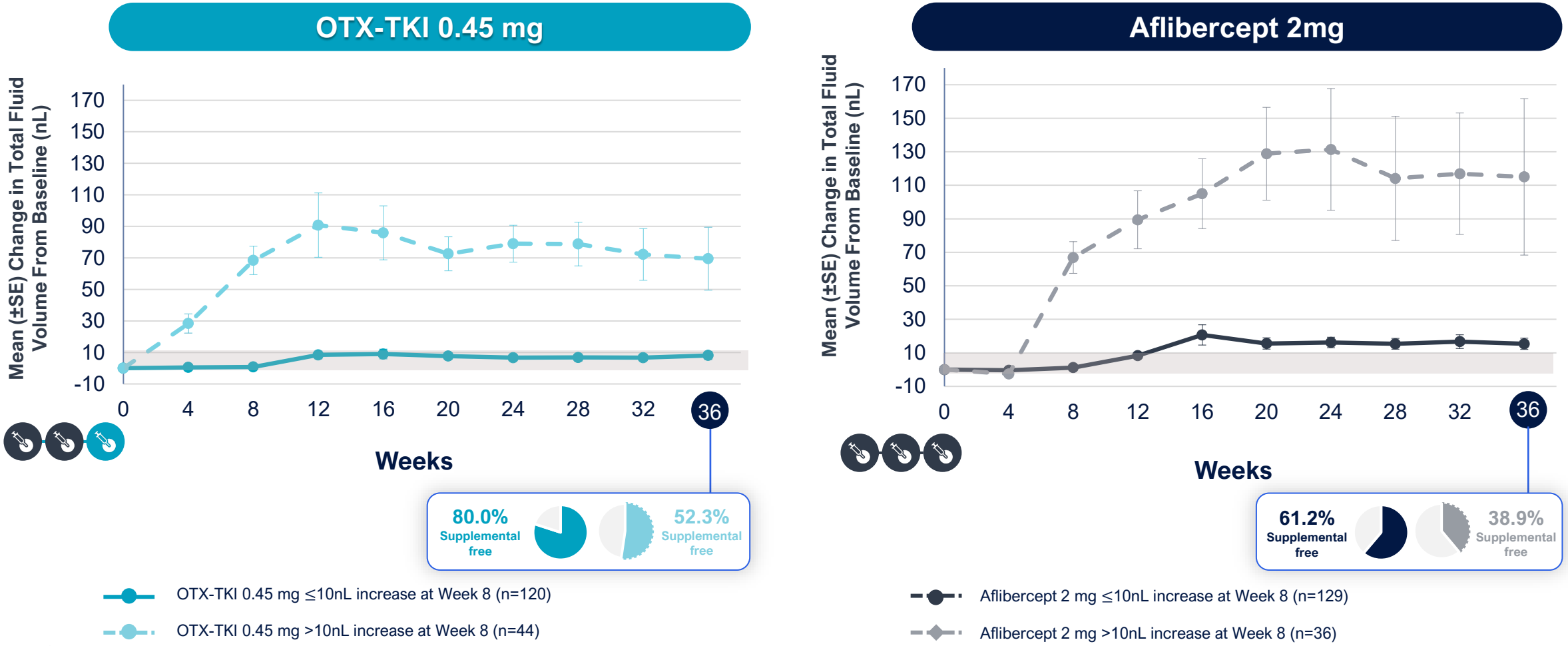
≤10nL increase
>10nL increase
Received supplemental treatment
Missing data

OCULAR THERAPEUTIX Retina experience redefined

*Approximately 70% of OTX-TKI–treated patients who were dry at Week 8 would achieve a 9-month dosing interval.
Quantitative dryness defined as total intraretinal fluid and subretinal fluid volume ≤10 nL on AI-based OCT evaluation with manual grader correction of retinal fluid performed at Boston Image Reading Center (BIRC). Analyses were based on observed cases. . For subjects who received supplemental treatment on or before Week 36, total retinal fluid measurements obtained after the first supplemental injection were treated as missing. Supplemental-free subjects include those who did not require rescue injections as specified by the protocol.
Wk, week; D, day; nL, nanoliter; AI, artificial intelligence

Patients With Early Fluid Control (~70%) Maintained Their Response through Week 36 with OTX-TKI with Minimal Variability

Post Hoc Analysis: Mean Change in Total Retinal Fluid Volume by Quantitative Dry Status at Week 8



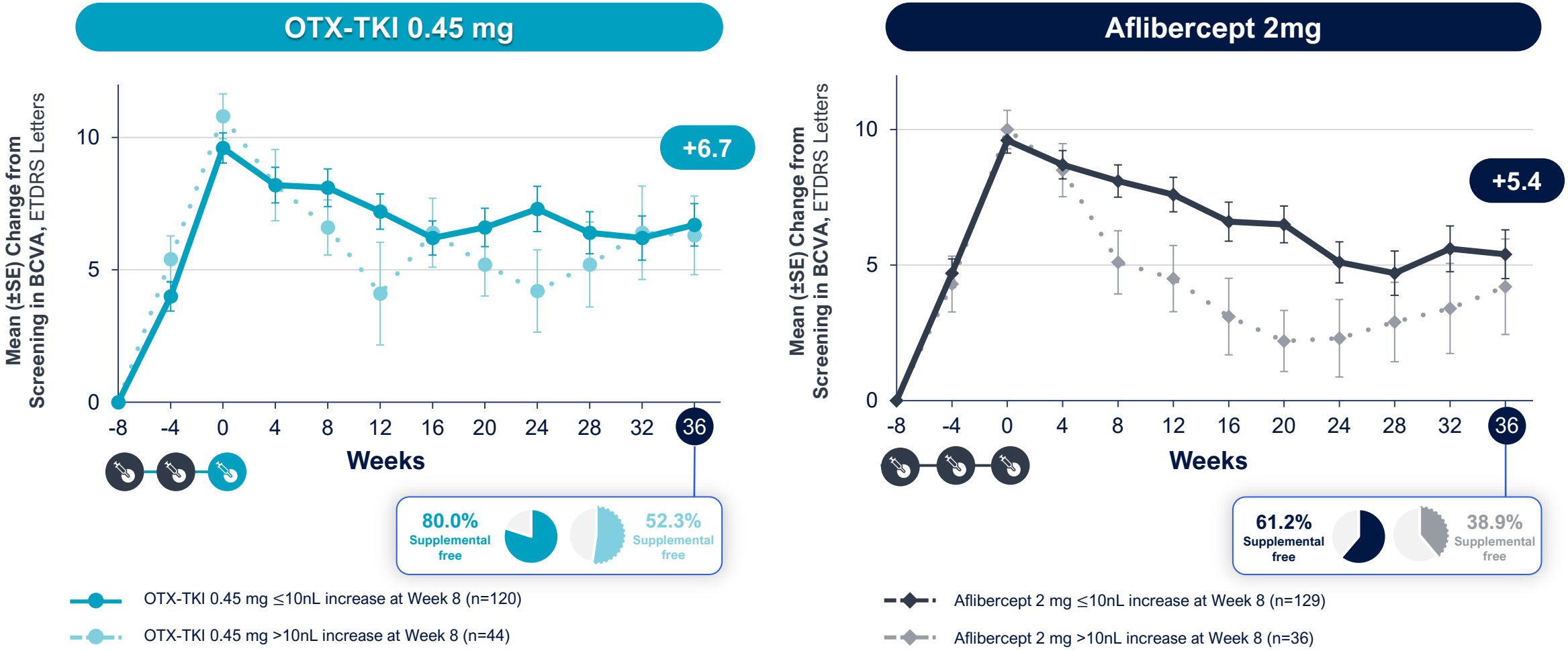
Quantitative dryness (Dry) defined as total intraretinal fluid and subretinal fluid volume ≤10 nL on AI-based OCT evaluation with manual grader correction of retinal fluid performed at Boston Image Reading Center (BIRC). Analyses were based on observed cases; data were missing for 6 participants in the OTX-TKI arm and 7 in the aflibercept arm at Week 8. For participants who received supplemental treatment on or before Week 36, fluid-volume measurements obtained after the first supplemental injection were treated as missing. Supplemental-free subjects include those who did not require rescue injections as specified by the protocol.

AI, artificial intelligence

Moshfeghi D. Presented at the American Academy of Ophthalmology Retina Subspecialty Day. October 9, 2026. New Orleans, LA

Patients With Early Fluid Control Demonstrated Sustained BCVA Outcomes with OTX-TKI

Post Hoc Analysis: Mean Change in BCVA by Quantitative Dry Status at Week 8



Quantitative dryness defined as total intraretinal fluid and subretinal fluid volume ≤10 nL on AI-based OCT evaluation with manual grader correction of retinal fluid performed at Boston Image Reading Center (BIRC). Analyses were based on observed cases; data were missing for 6 participants in the OTX-TKI arm and 7 in the aflibercept arm at Week 8. For subjects who received supplemental treatment on or before Week 36, BCVA measurements obtained after the first supplemental injection were treated as missing. Supplemental-free subjects include those who did not require rescue injections as specified by the protocol.
BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study

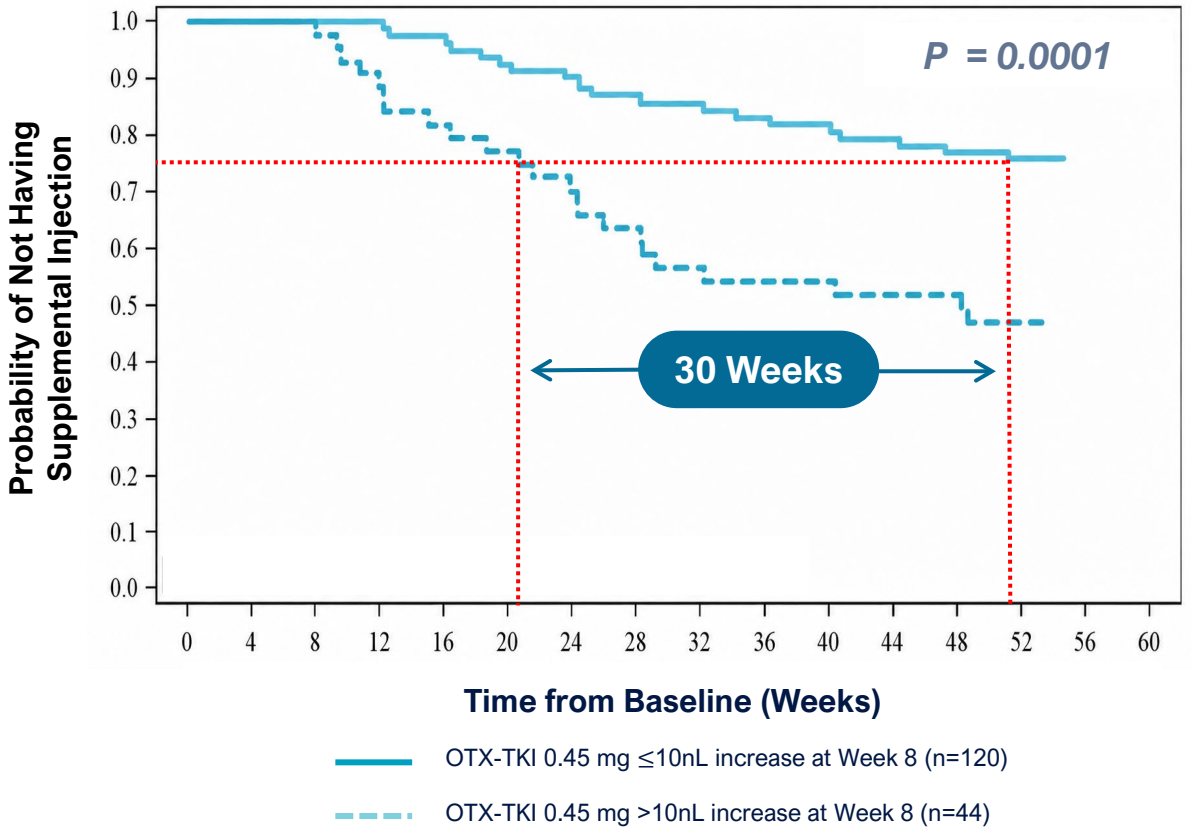
Moshfeghi D. Presented at the American Academy of Ophthalmology Retina Subspecialty Day. October 9, 2026. New Orleans, LA

Early Persistent Fluid Associated with Significantly Earlier Supplemental Treatment

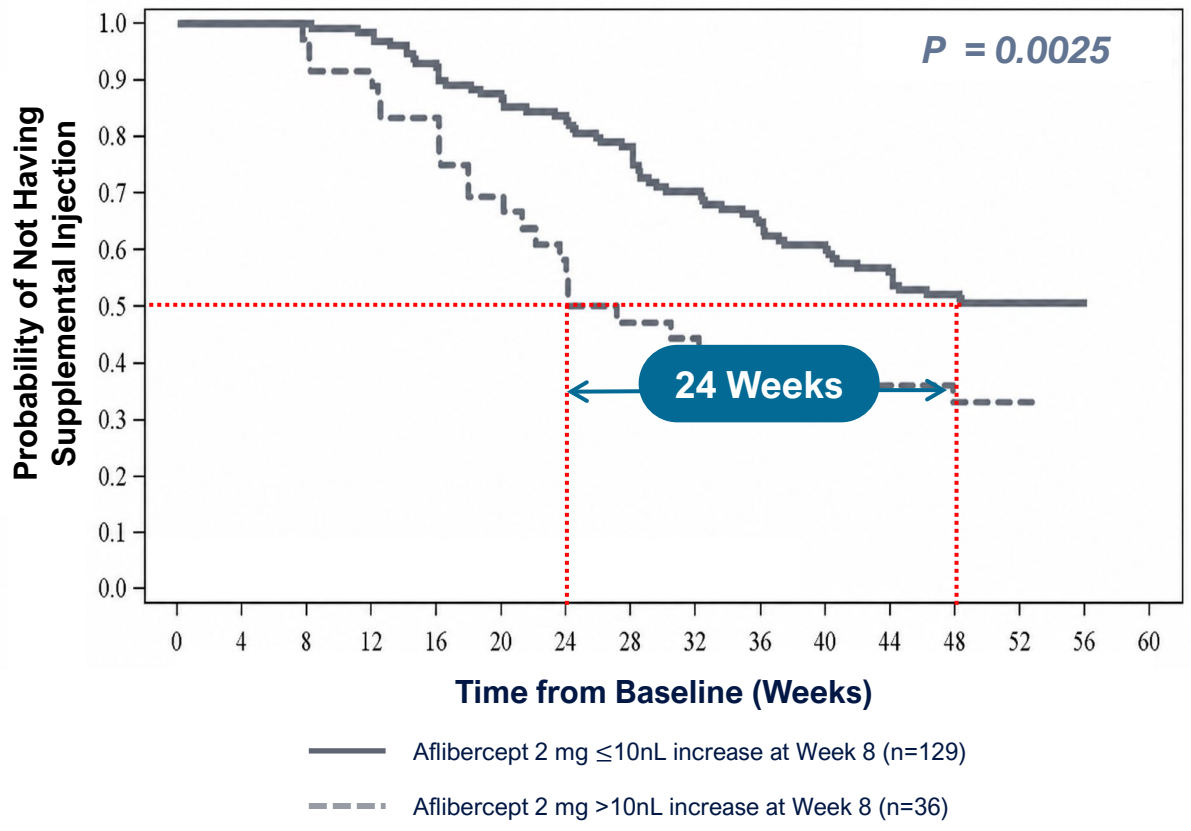
Post Hoc Analysis: Time to Supplemental Treatment by Quantitative Dry Status at Week 8

SOL-1

OTX-TKI 0.45 mg



Aflibercept 2mg



OCULAR THERAPEUTIX Retina experience redefined™

Analyses were based on observed cases; data were missing for 6 subjects in the OTX-TKI arm and 7 in the aflibercept arm at Week 8.

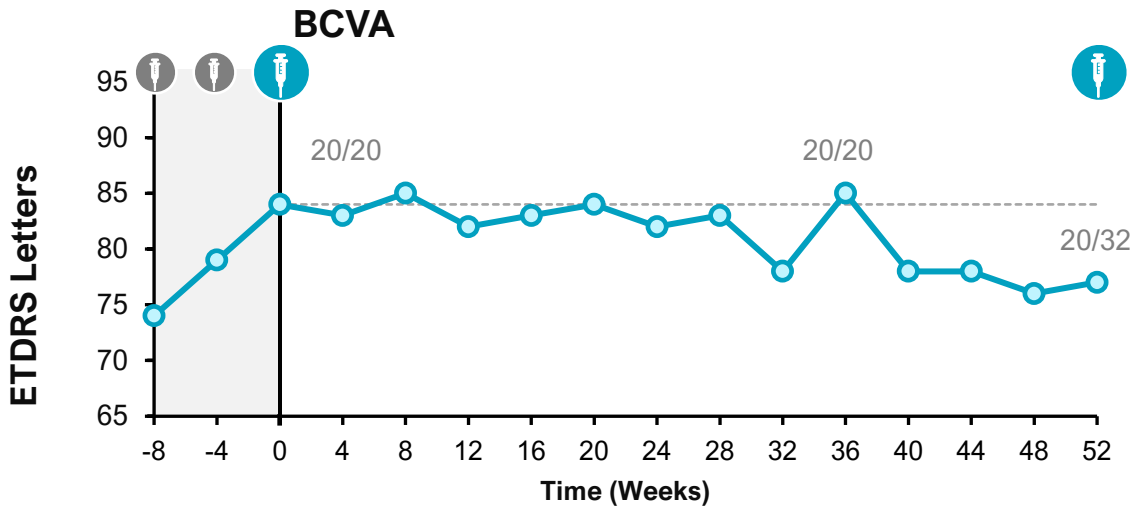
SOL-1

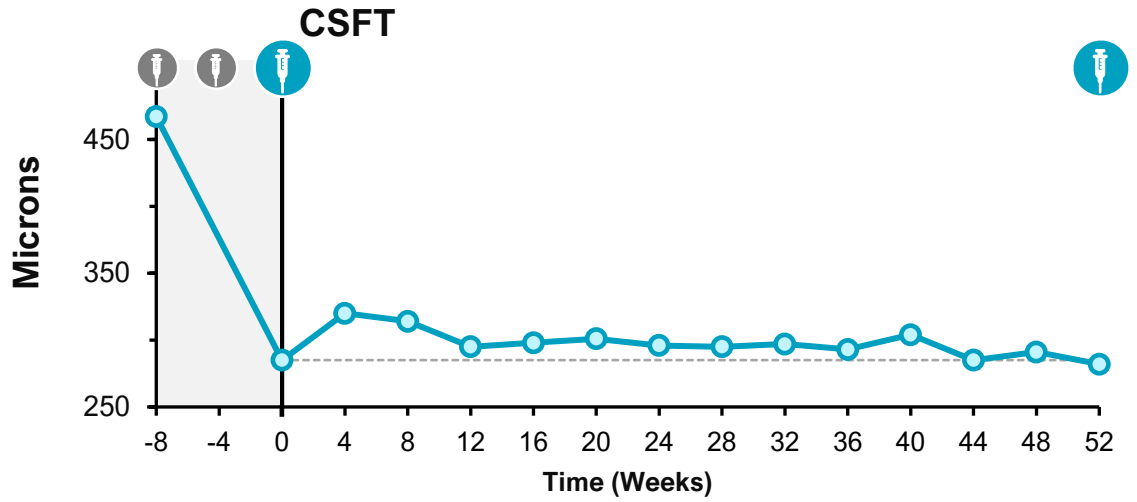
Clinical Evidence

Mark R. Barakat MD, FASRS

OCULAR THERAPEUTIX Retina experience redefined

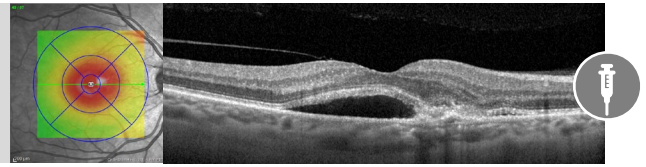
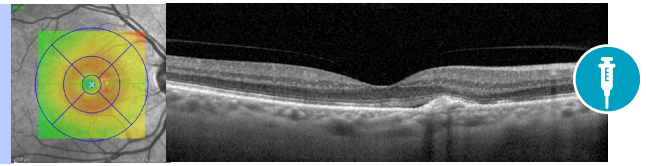
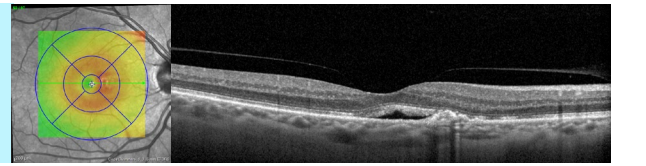
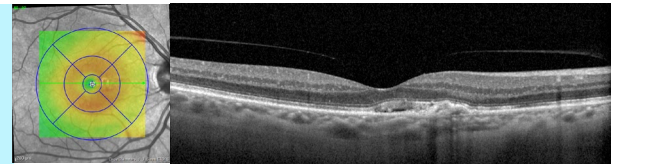
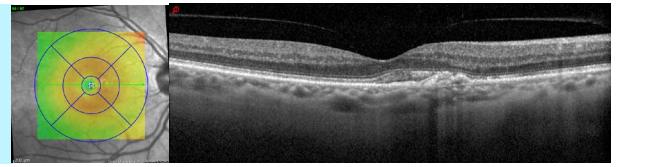
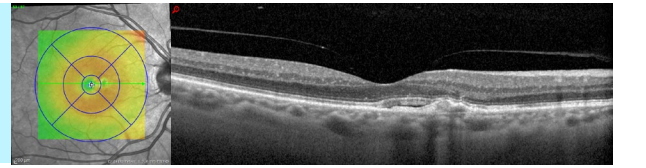
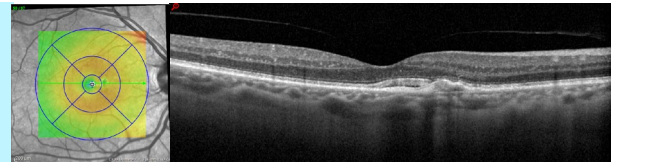
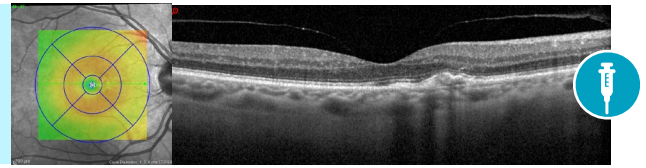
OTX-TKI Case 1





Screening Aflibercept (2mg)

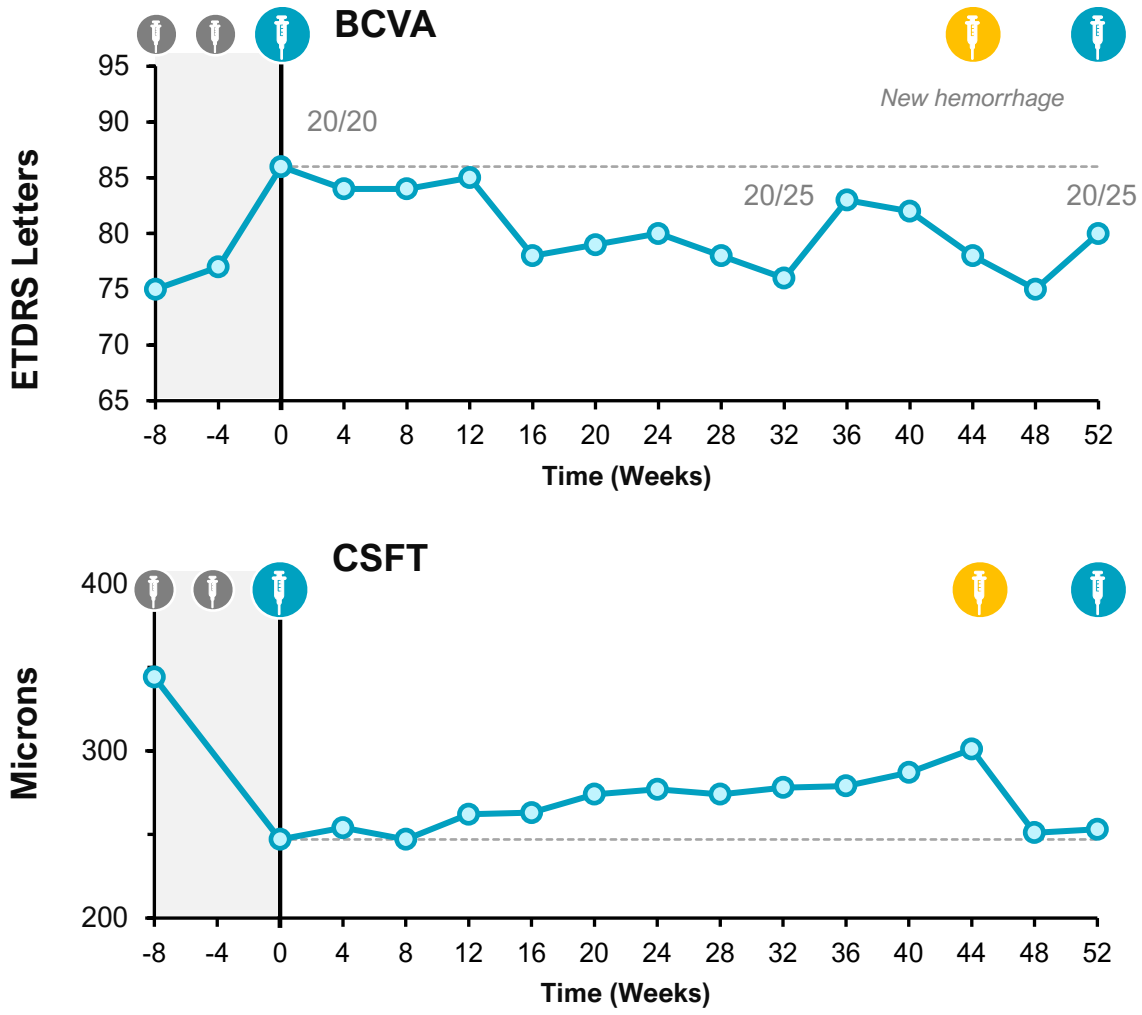
OTX-TKI (0.45mg)

-8 Weeks	**BCVA:** 74 Ltrs (-10) **CSFT:** 467 µm	
Baseline	**BCVA:** 84 Ltrs *Snellen: 20/20* **CSFT:** 285 µm	
Week 4	**BCVA (Δ):** 83 (-1) Ltrs **CSFT (Δ):** 320 (+35) µm	
Week 12	**BCVA (Δ):** 82 (-2) Ltrs **CSFT (Δ):** 295 (+10) µm	
Week 24	**BCVA (Δ):** 82 (-2) Ltrs **CSFT (Δ):** 296 (+11) µm	
Week 36	**BCVA (Δ):** 85 (+1) Ltrs *Snellen: 20/20* **CSFT (Δ):** 293 (+8) µm	
Week 44	**BCVA (Δ):** 78 (-6) Ltrs **CSFT (Δ):** 285 (0) µm	
Week 52	**BCVA (Δ):** 77 (-7) Ltrs *Snellen: 20/32* **CSFT (Δ):** 282 (-3) µm	

OCULAR THERAPEUTIX Retina experience redefined

Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

OTX-TKI Case 2

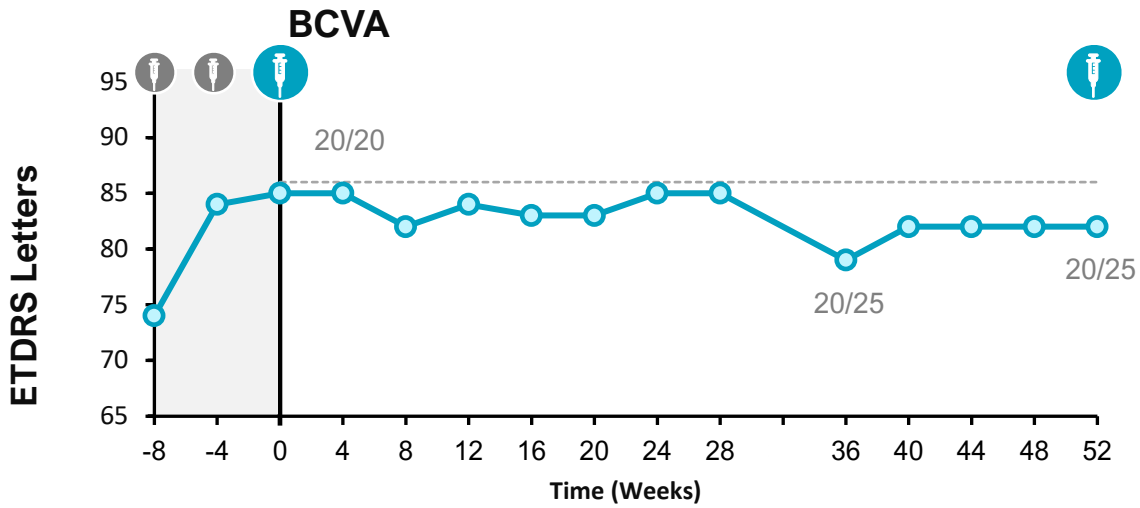


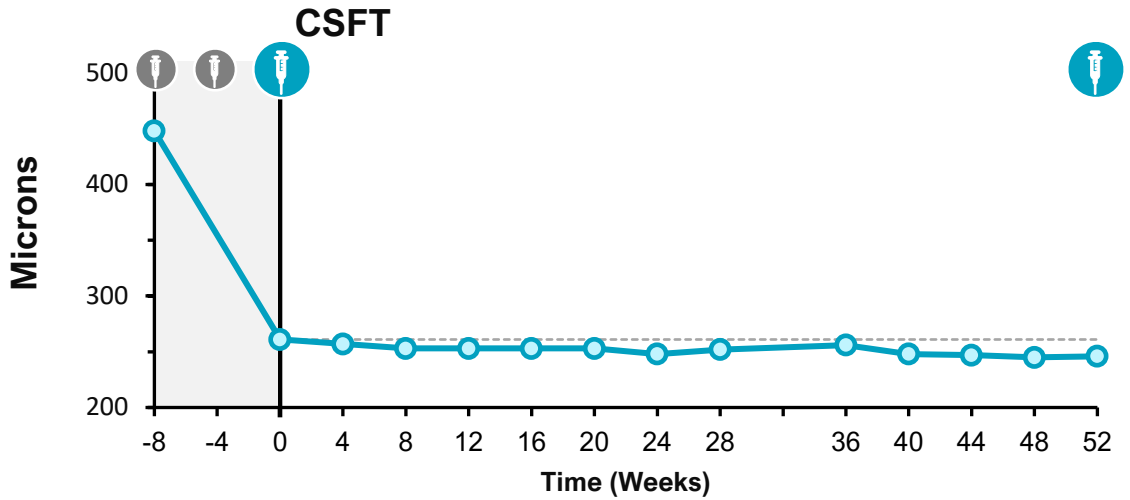
-8 Weeks	**BCVA:** 75 Ltrs **CSFT:** 344 µm	
Baseline	**BCVA:** 86 Ltrs *Snellen: 20/20* **CSFT:** 247 µm	
Week 4	**BCVA (Δ):** 84 (-2) Ltrs **CSFT (Δ):** 254 (+7) µm	
Week 12	**BCVA (Δ):** 85 (-1) Ltrs **CSFT (Δ):** 262 (+15) µm	
Week 24	**BCVA (Δ):** 80 (-6) Ltrs **CSFT (Δ):** 277 (+30) µm	
Week 36	**BCVA (Δ):** 83 (-3) Ltrs *Snellen: 20/25* **CSFT (Δ):** 279 (+32) µm	
Week 44	**BCVA (Δ):** 78 (-8) Ltrs **CSFT (Δ):** 301 (+54) µm	
Week 52	**BCVA (Δ):** 80 (-6) Ltrs *Snellen: 20/25* **CSFT (Δ):** 253 (+6) µm	

OCULAR THERAPEUTIX Retina experience redefined

Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

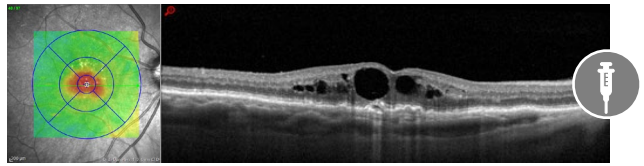
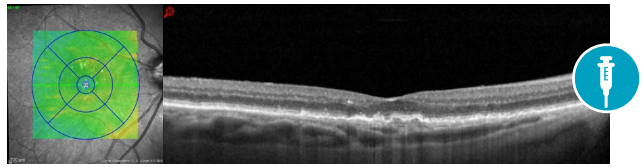
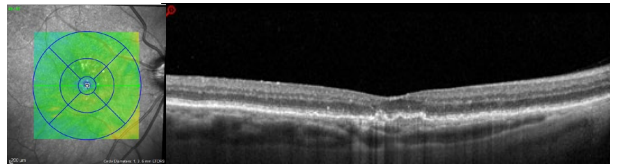
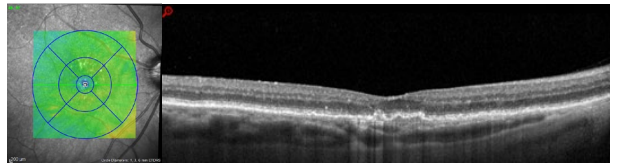
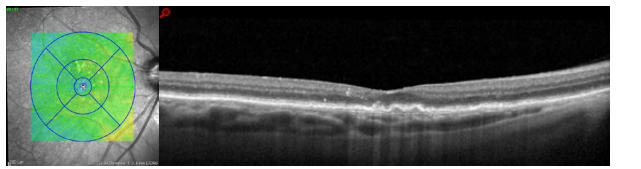
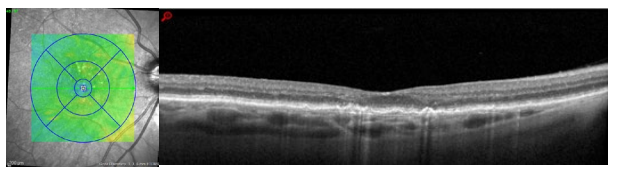
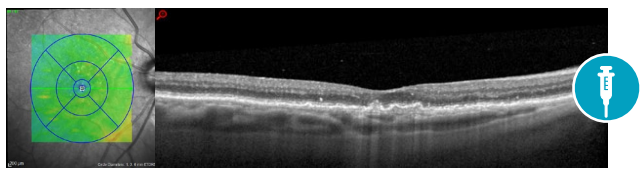
OTX-TKI Case 3





Screening
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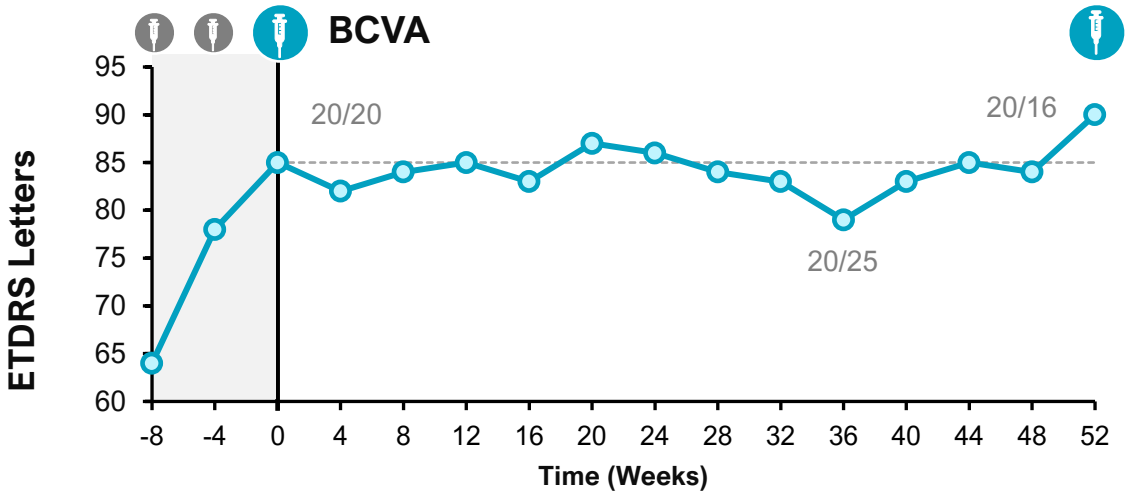
OTX-TKI
(0.45mg)

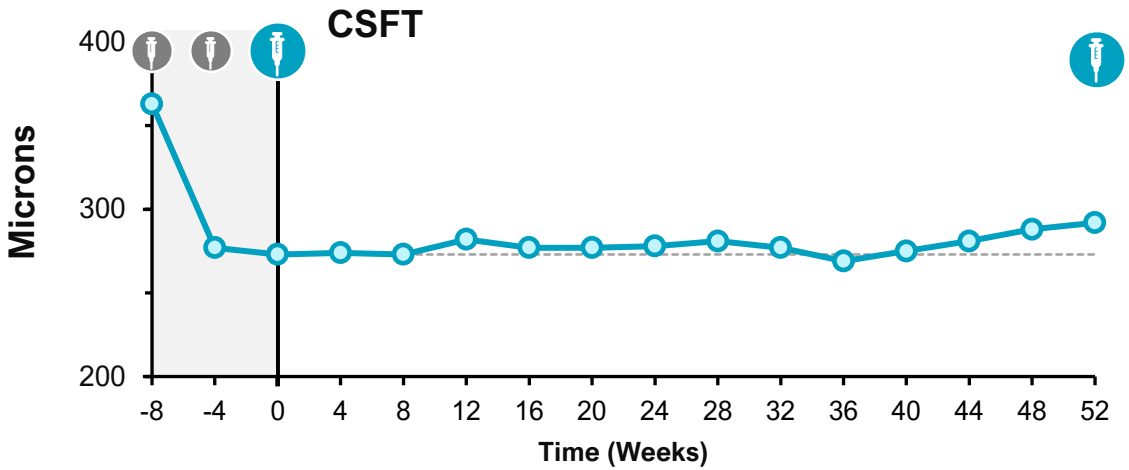
-8 Weeks	**BCVA:** 74 Ltrs **CSFT:** 448 µm	
Baseline	**BCVA:** 85 Ltrs *Snellen: 20/20* **CSFT:** 261 µm	
Week 4	**BCVA (Δ):** 85 (0) Ltrs **CSFT (Δ):** 257 (-4) µm	
Week 12	**BCVA (Δ):** 84 (-1) Ltrs **CSFT (Δ):** 253 (-8) µm	
Week 24	**BCVA (Δ):** 85 (0) Ltrs **CSFT (Δ):** 248 (-13) µm	
Week 36	**BCVA (Δ):** 79 (-6) Ltrs *Snellen: 20/25* **CSFT (Δ):** 256 (-5) µm	
Week 52	**BCVA (Δ):** 82 (-3) Ltrs *Snellen: 20/25* **CSFT (Δ):** 246 (-15) µm	

OCULAR THERAPEUTIX
Retina experience redefined

Subject missed Week 32 visit
Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

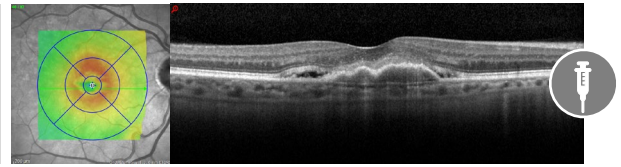
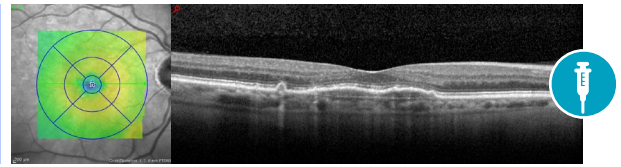
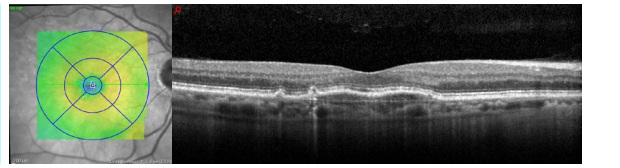
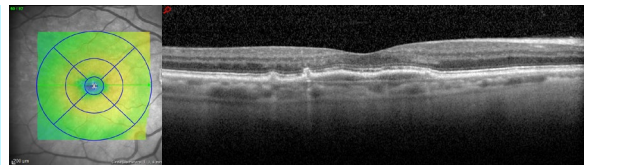
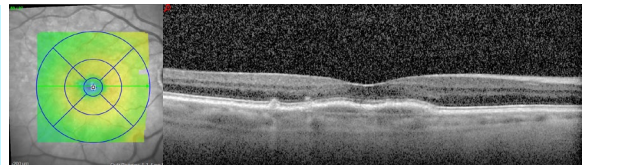
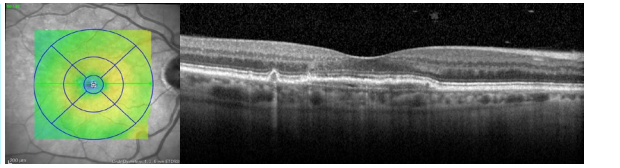
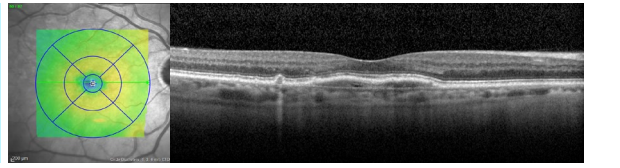
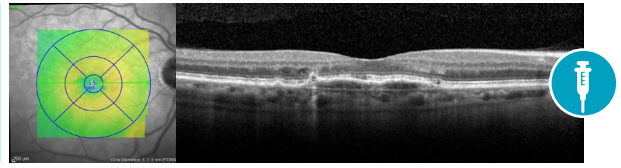
OTX-TKI Case 4





Screening
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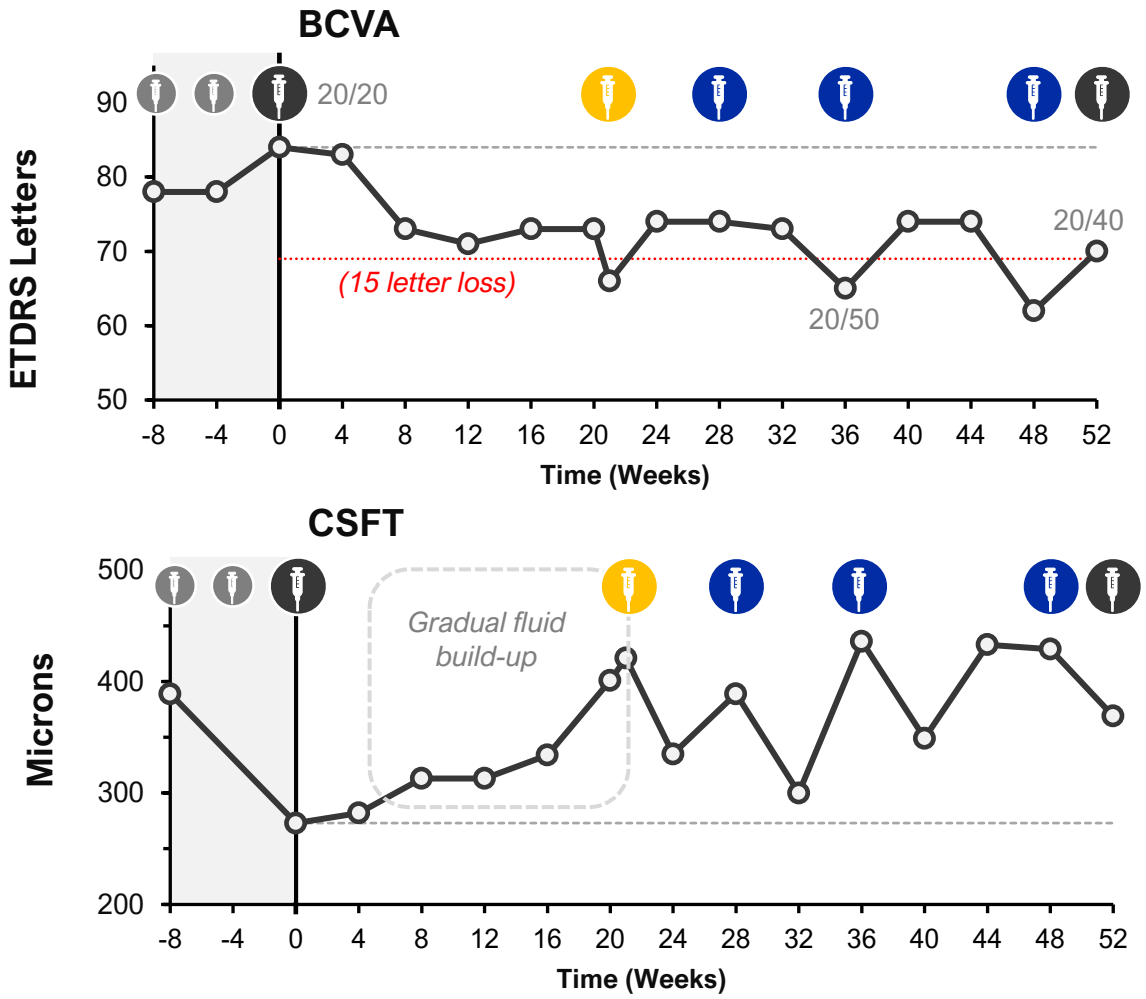
OTX-TKI
(0.45mg)

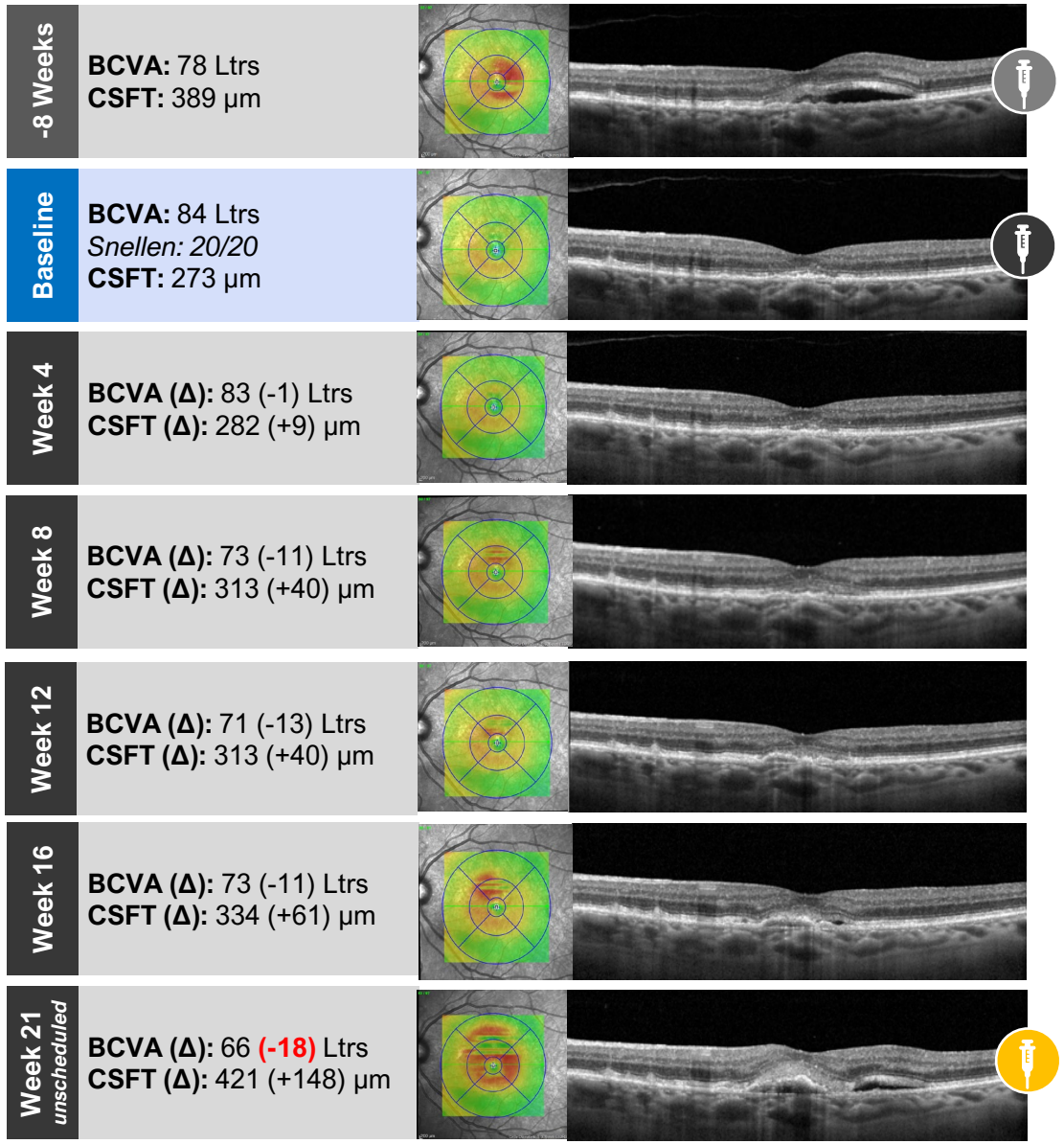
-8 Weeks	**BCVA:** 64 Ltrs **CSFT:** 363 µm	
Baseline	**BCVA:** 85 Ltrs *Snellen: 20/20* **CSFT:** 273 µm	
Week 4	**BCVA (Δ):** 82 (-3) Ltrs **CSFT (Δ):** 274 (+1) µm	
Week 16	**BCVA (Δ):** 83 (-2) Ltrs **CSFT (Δ):** 277 (+4) µm	
Week 24	**BCVA (Δ):** 86 (+1) Ltrs **CSFT (Δ):** 278 (+5) µm	
Week 36	**BCVA (Δ):** 79 (-6) Ltrs *Snellen: 20/26* **CSFT (Δ):** 269 (-4) µm	
Week 44	**BCVA (Δ):** 85 (0) Ltrs **CSFT (Δ):** 281 (+8) µm	
Week 52	**BCVA (Δ):** 90 (+5) Ltrs *Snellen: 20/16* **CSFT (Δ):** 292 (+19) µm	

OCULAR THERAPEUTIX
Retina experience redefined

Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

Aflibercept Case 1





OCULAR THERAPEUTIX Retina experience redefined

Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

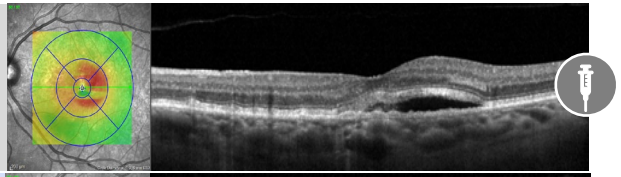
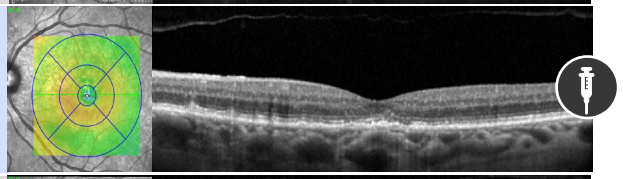
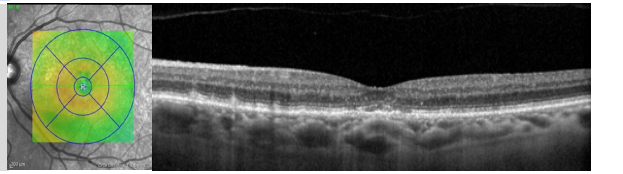
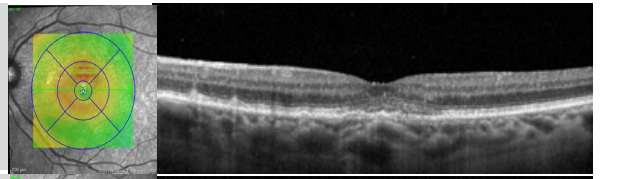
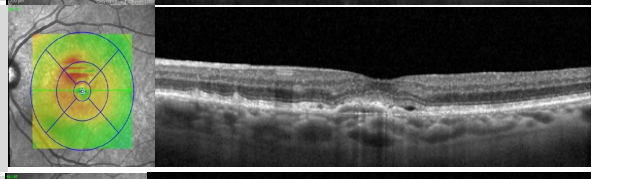
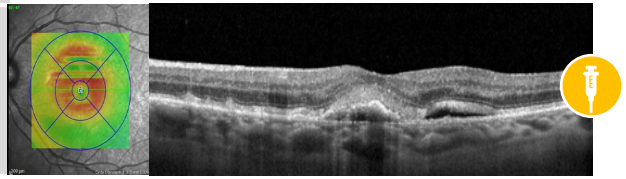
Aflibercept Case 1

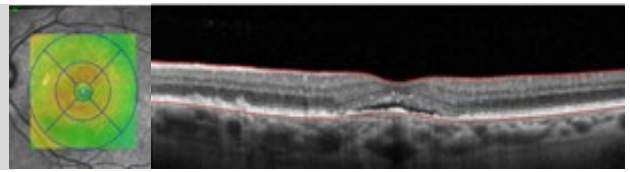
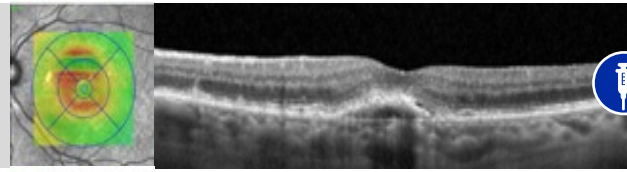
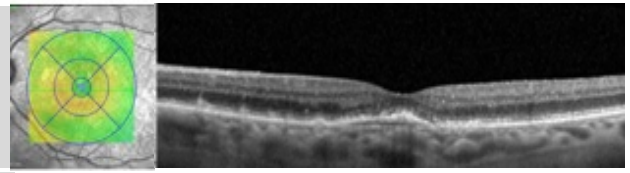
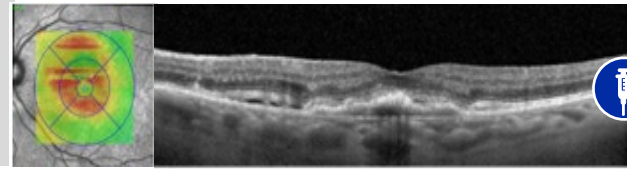
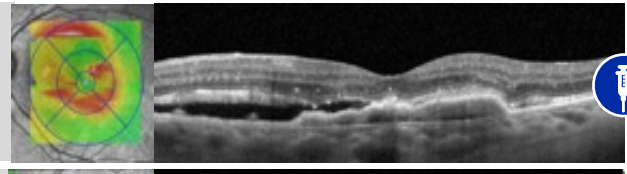
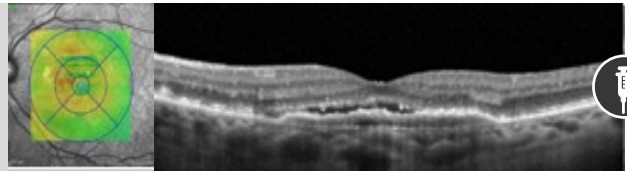
Screening Aflibercept (2mg)

Study Aflibercept (2 mg)

Per-Protocol Supplemental Aflibercept (2mg)

Investigator Discretion Supplemental

-8 Weeks	**BCVA:** 78 Ltrs **CSFT:** 389 µm	
Baseline	**BCVA:** 84 Ltrs *Snellen: 20/20* **CSFT:** 273 µm	
Week 4	**BCVA (Δ):** 83 (-1) Ltrs **CSFT (Δ):** 282 (+9) µm	
Week 8	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 313 (+40) µm	
Week 16	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 334 (+61) µm	
Week 21 *unscheduled*	**BCVA (Δ):** 66 (-18) Ltrs **CSFT (Δ):** 421 (+148) µm	

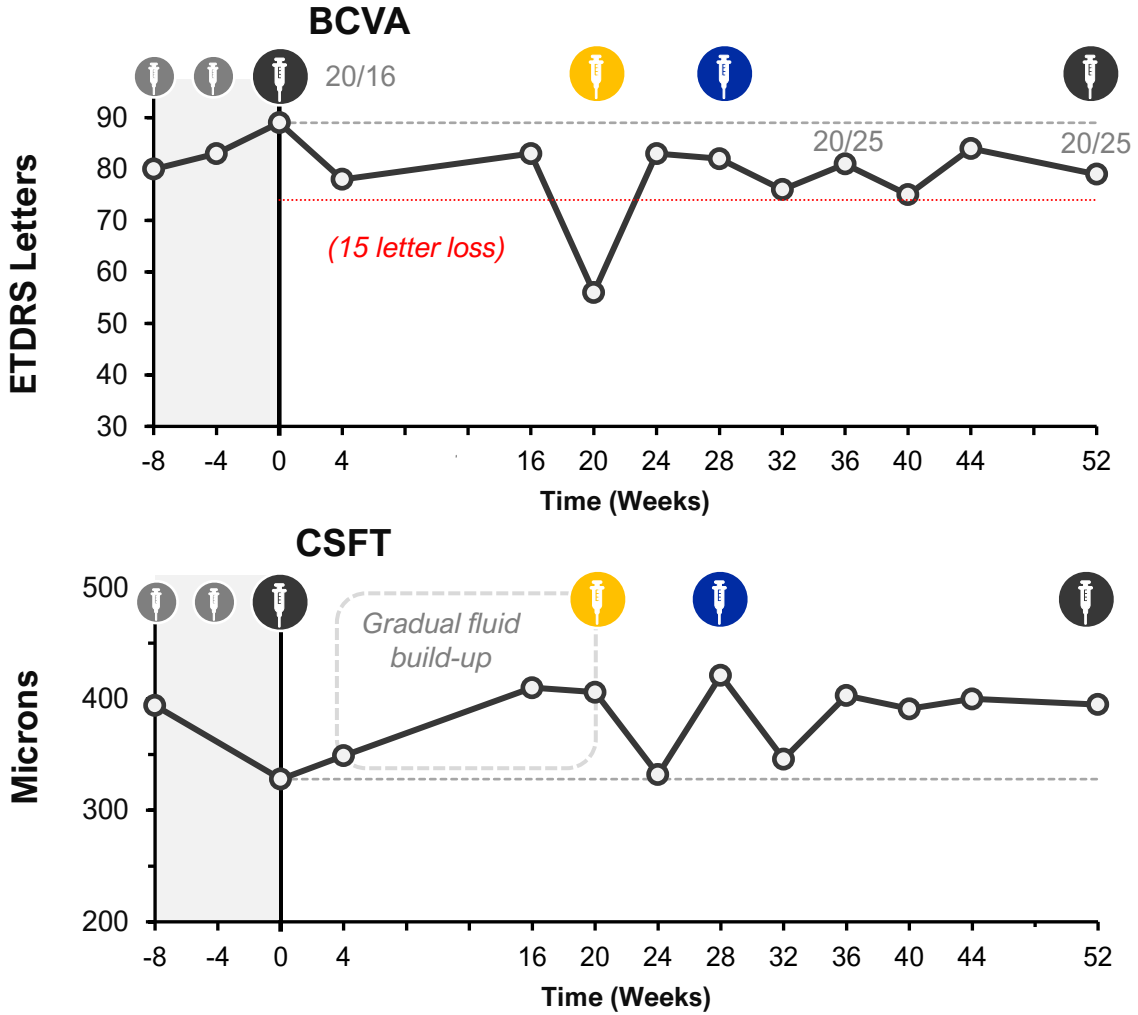
Week 24	**BCVA (Δ):** 74 (-10) Ltrs **CSFT (Δ):** 335 (+62) µm	
Week 28	**BCVA (Δ):** 74 (-10) Ltrs **CSFT (Δ):** 389 (+116) µm	
Week 32	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 300 (+27) µm	
Week 36	**BCVA (Δ):** 65 (-19) Ltrs *Snellen: 20/50* **CSFT (Δ):** 436 (+163) µm	
Week 48	**BCVA (Δ):** 62 (-22) Ltrs **CSFT (Δ):** 429 (+156) µm	
Week 52	**BCVA (Δ):** 70 (-14) Ltrs *Snellen: 20/40* **CSFT (Δ):** 369 (+96) µm	

OCULAR THERAPEUTIX Retina experience redefined

Case study of one subject; individual results may vary

BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

Aflibercept Case 2



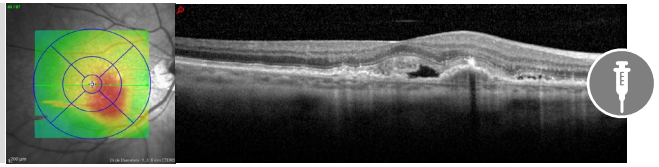
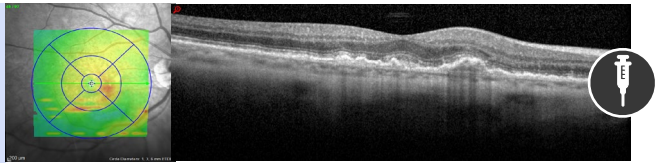
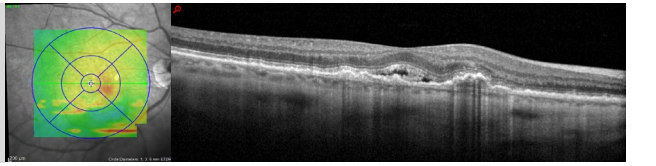
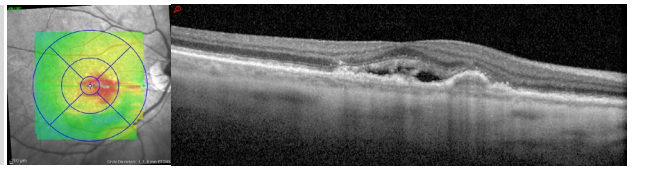
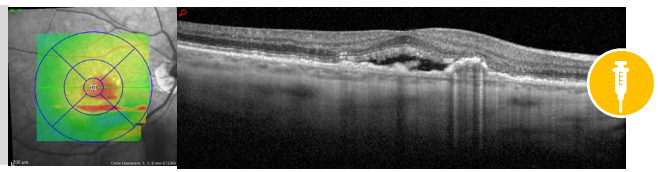
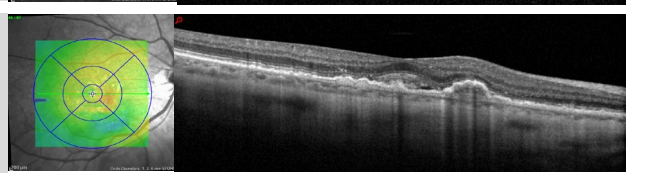
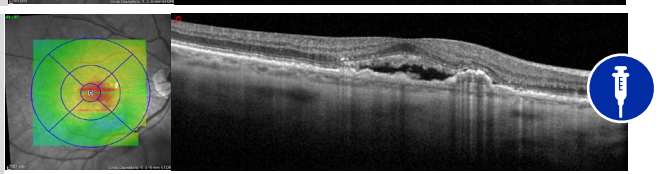
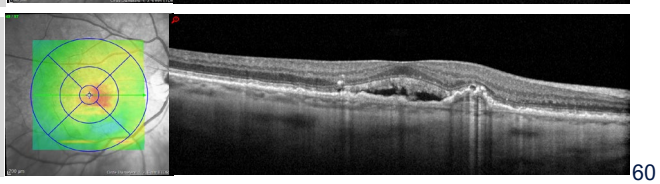
Screening Aflibercept (2mg)

Study Aflibercept (2 mg)

Per-Protocol Supplemental Aflibercept (2mg)

Investigator Discretion Supplemental

OCULAR THERAPEUTIX Retina experience redefined

-8 Weeks	**BCVA:** 80 Ltrs **CSFT:** 394 µm	
Baseline	**BCVA:** 89 Ltrs *Snellen: 20/16* **CSFT:** 328 µm	
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Week 28	**BCVA (Δ):** 82 (-7) Ltrs **CSFT (Δ):** 421 (+93) µm	
Week 36	**BCVA (Δ):** 81(-8) Ltrs *Snellen: 20/25* **CSFT (Δ):** 403 (+75) µm	

Subject missed W8/W12/W48 Visits
Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

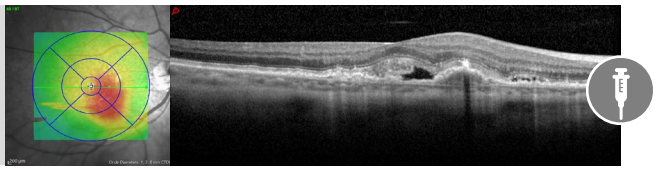
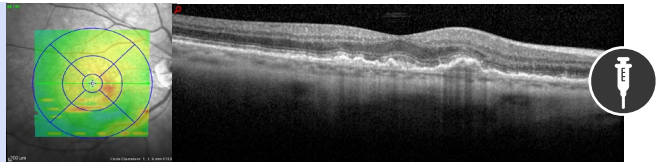
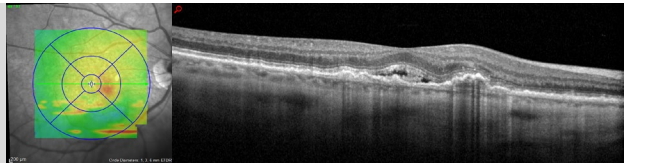
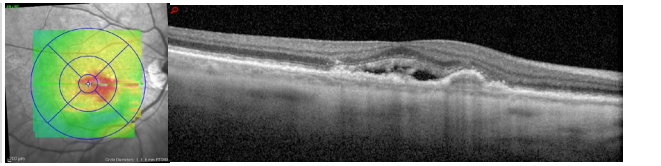
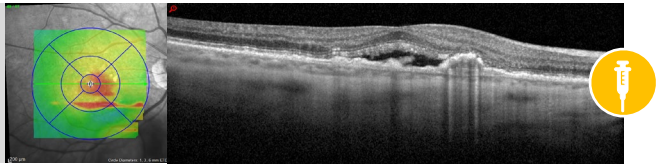
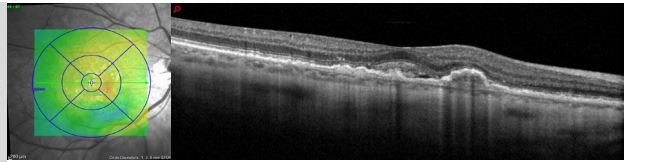
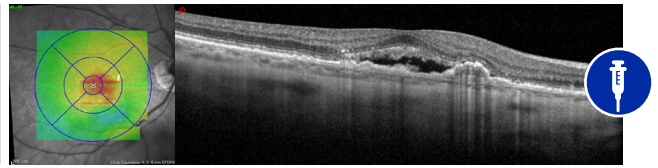
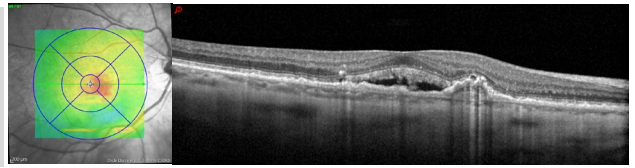
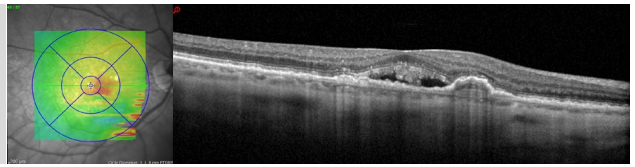
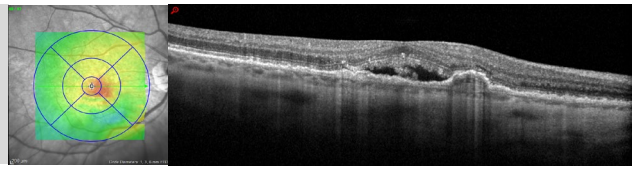
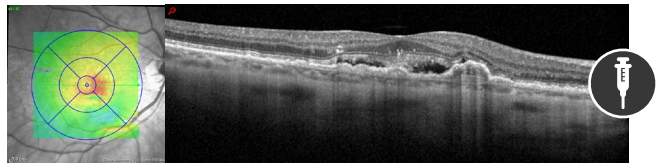
Aflibercept Case 2

Screening Aflibercept (2mg) injection

Study Aflibercept (2 mg) administration

Per-Protocol Supplemental Aflibercept (2mg)

Investigator Discretion Supplemental

-8 Weeks	**BCVA:** 80 Ltrs **CSFT:** 394 µm	
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Week 40	**BCVA (Δ):** 75 (-14) Ltrs **CSFT (Δ):** 391 (+63) µm	
Week 44	**BCVA (Δ):** 84 (-5) Ltrs **CSFT (Δ):** 400 (+72) µm	
Week 52	**BCVA (Δ):** 79 (-10) Ltrs *Snellen: 20/25* **CSFT (Δ):** 395 (+67) µm	

OCULAR THERAPEUTIX Retina experience redefined

Subject missed W8/W12/W48 Visits
Case study of one subject; individual results may vary
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Ltrs, letters

Driving Clinical Development Through Evidence-Based Strategy

Jeffrey S. Heier, MD, FASRS



Timeline to OTX-TKI NDA Submission Package for nAMD

Feb 2026 — **Positive SOL-1 Week 52 results** announced on February 17, 2026

May 2026 — **Early Alignment at Type C Meeting:**
FDA agreed in writing on NDA submission with SOL-1 trial plus confirmatory evidence

Sept 2026 — **Pre-NDA meeting:**
Aligned on format and content of information to be submitted in NDA

4Q 2026 — **SOL-R interim 52-week safety database lock** to reach >300 patients who received OTX-TKI with repeat dosing planned

4Q 2026 — **OTX-TKI NDA package to be submitted to FDA**

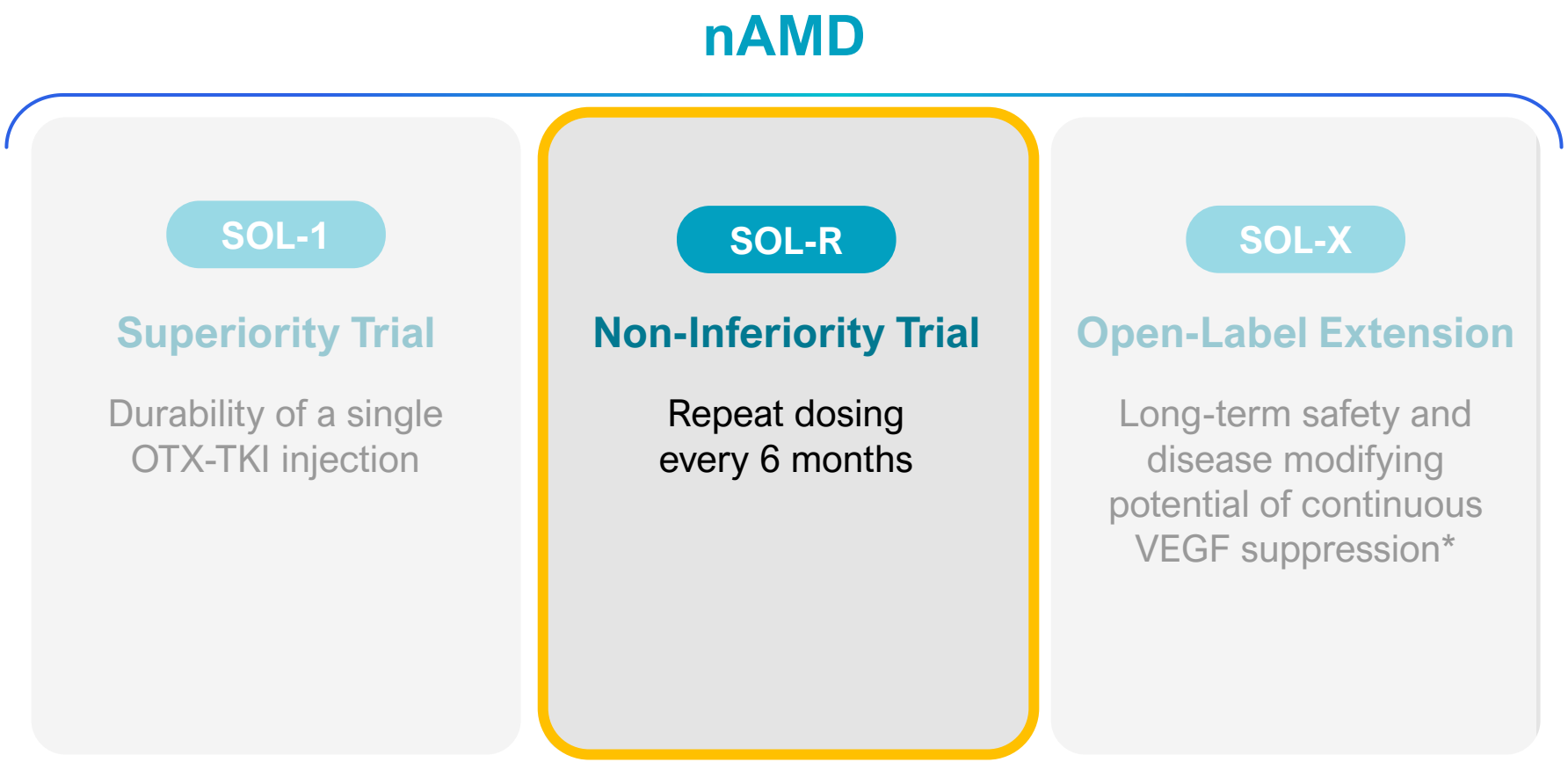
Post-NDA — **Year 2 Safety from SOL-1**
Intended to support repeat dosing to be submitted at 120-day safety update

OCULAR THERAPEUTIX Retina experience redefined

NDA, New Drug Application

OTX-TKI Phase 3 Clinical Programs

Evaluating the efficacy, durability, and safety of OTX-TKI in nAMD



OCULAR THERAPEUTIX Retina experience redefined™

nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor

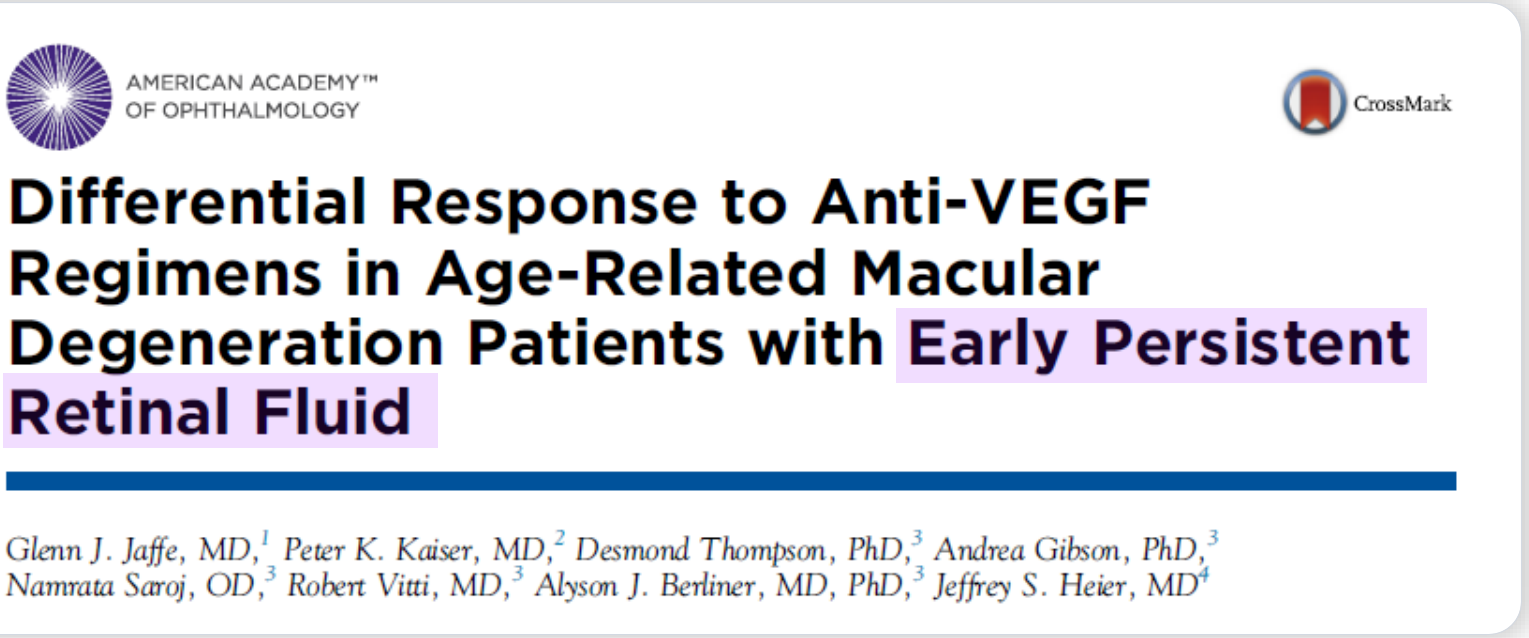
*Eligible patients who complete end of Year 2 visit in SOL-1 or SOL-R

Core Considerations in Wet AMD Patient Selection From OCUL Perspective

Wet AMD Patient Selection

Early persistent fluid and fluctuations are an indicator of highly variable disease and worse visual outcomes[1,2]

SOL-R randomized population enriched for stable aVEGF response to increase likelihood of success



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CrossMark

Differential Response to Anti-VEGF Regimens in Age-Related Macular Degeneration Patients with Early Persistent Retinal Fluid

Glenn J. Jaffe, MD,[1] Peter K. Kaiser, MD,[2] Desmond Thompson, PhD,[3] Andrea Gibson, PhD,[3] Namrata Saroj, OD,[3] Robert Vitti, MD,[3] Alyson J. Berliner, MD, PhD,[3] Jeffrey S. Heier, MD[4]

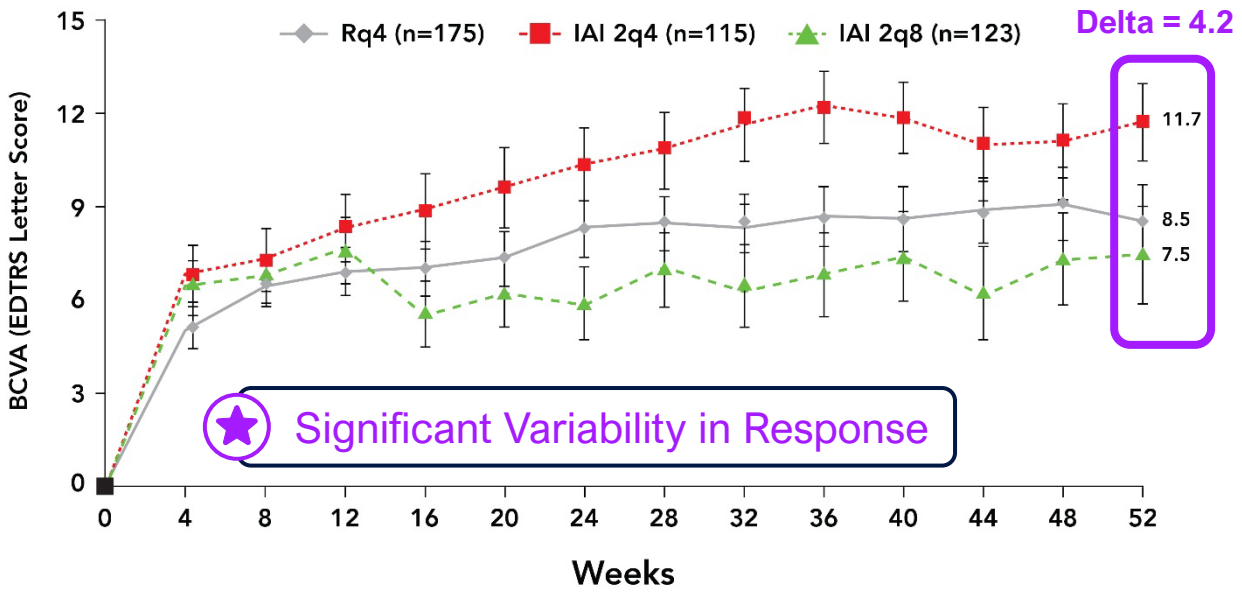
OCULAR THERAPEUTIX Retina experience redefined™

1. Evans RN, et al. *JAMA Ophthalmol*. 2020;138(10):1043-1051; 2. Jaffe GJ, et al. *Ophthalmology*. 2016;123(9):1856-1864.
AMD, age-related macular degeneration; OCUL, Ocular Therapeutix

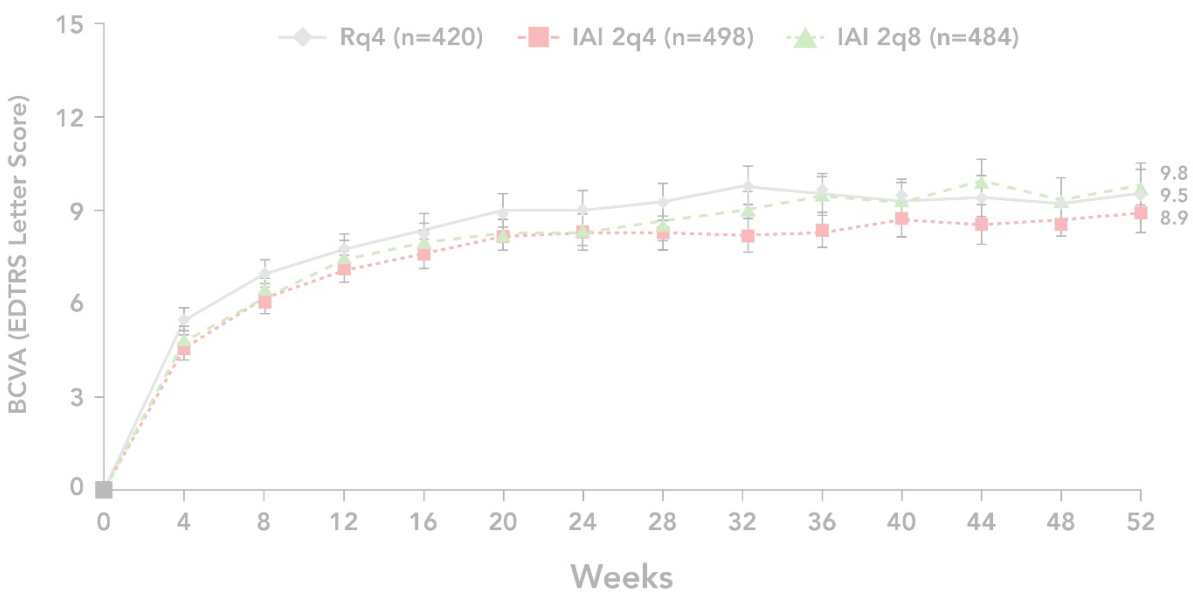
Patients with Early Persistent Fluid Can Disrupt Non-Inferiority Trials

Early persistent fluid patients are excluded from SOL-R

Vision in Patients *with* Early Persistent Fluid[1]



Vision in Patients *without* Early Persistent Fluid[1]



In patients with early persistent fluid, **monthly AFL 2mg provided significant additional clinical benefit** over AFL 2mg dosed every 8 weeks or monthly ranibizumab.[1]

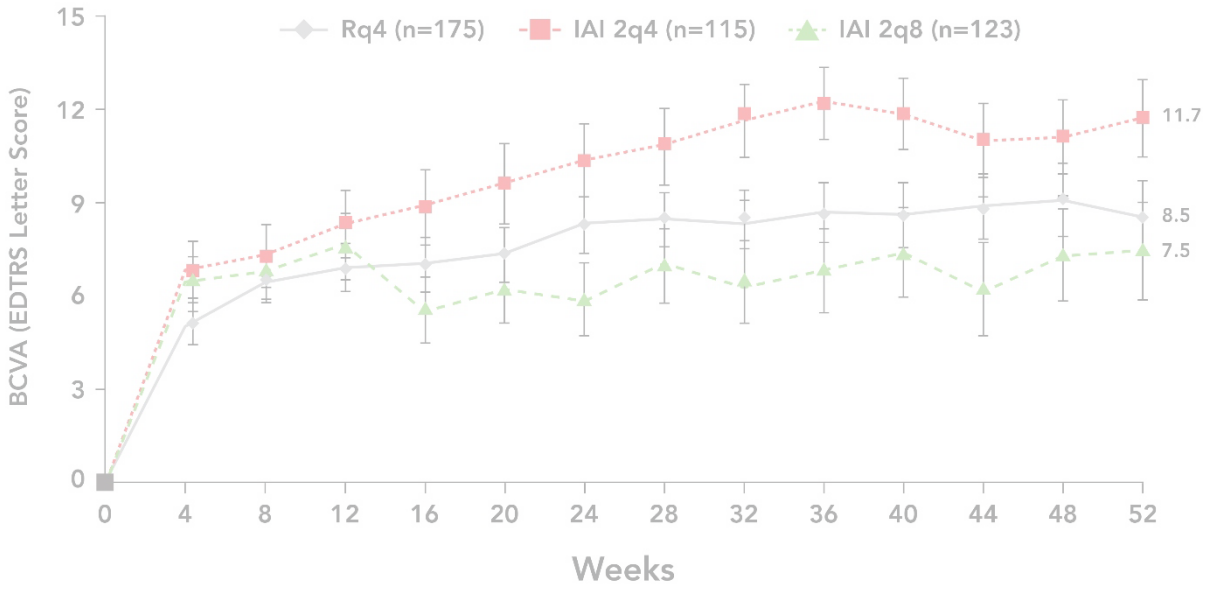
OCULAR THERAPEUTIX Retina experience redefined™

Figures adapted from Jaffe et al.[1]
Rq4, ranibizumab every 4 weeks; IAI 2q4/8, intravitreal aflibercept injection 2mg every 4/8 weeks
"Early Persistent Fluid" group captures patients that had retinal fluid as defined earlier on all initial 4 visits (baseline and weeks 4, 8, and 12). This period included all 3 visits during the initial loading dose period when all eyes were treated every 4 weeks, as well as 4 weeks after the third treatment. 1. Jaffe GJ, et al. *Ophthalmology*. 2016;123(9):1856-1864.
BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; AFL. aflibercept

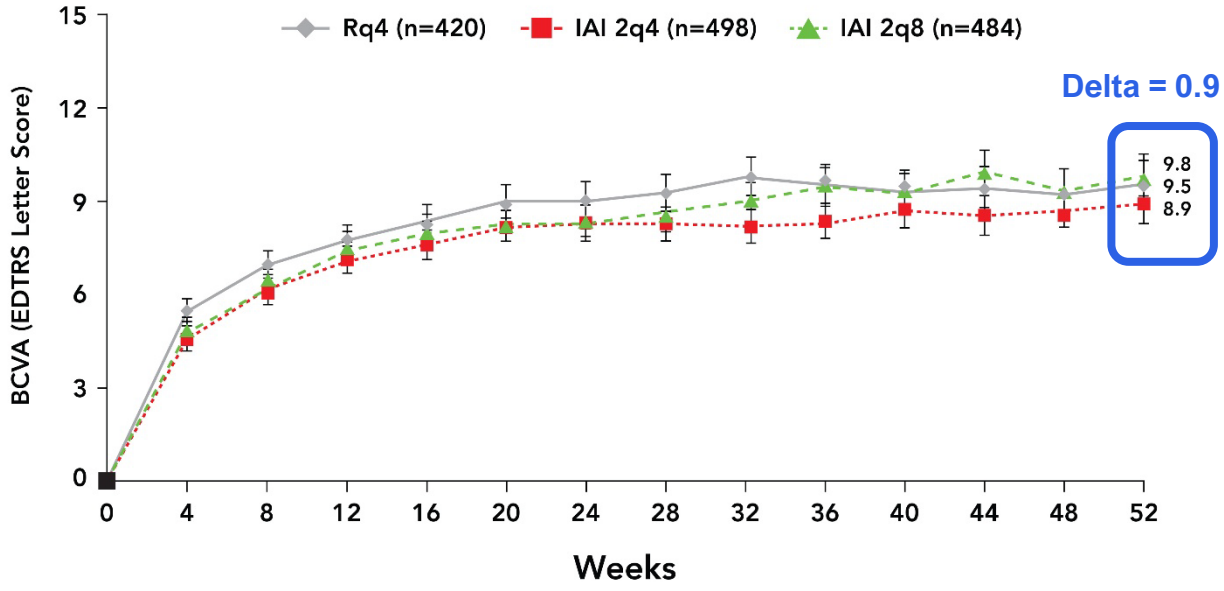
Patients with Early Persistent Fluid Can Disrupt Non-Inferiority Trials

Early persistent fluid patients are excluded from SOL-R

✗ Vision in Patients *with* Early Persistent Fluid[1]



✓ Vision in Patients *without* Early Persistent Fluid[1]



Screening criteria **excluding subjects with early persistent fluid** may be critical for trial success

Retina experience redefined™

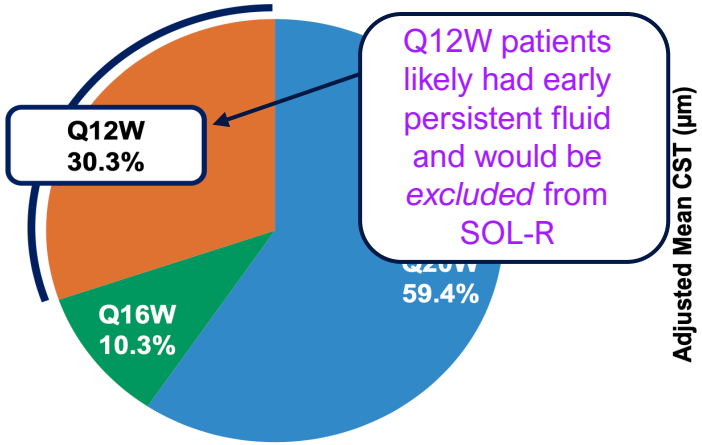
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BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; AFL. aflibercept

Lessons From KODIAK's DAZZLE Study: Rationale for SOL-R Patient Selection

DAZZLE Trial Did Not Meet Primary Endpoint[1]
Original Zenkuda/KSI-301 Formulation*

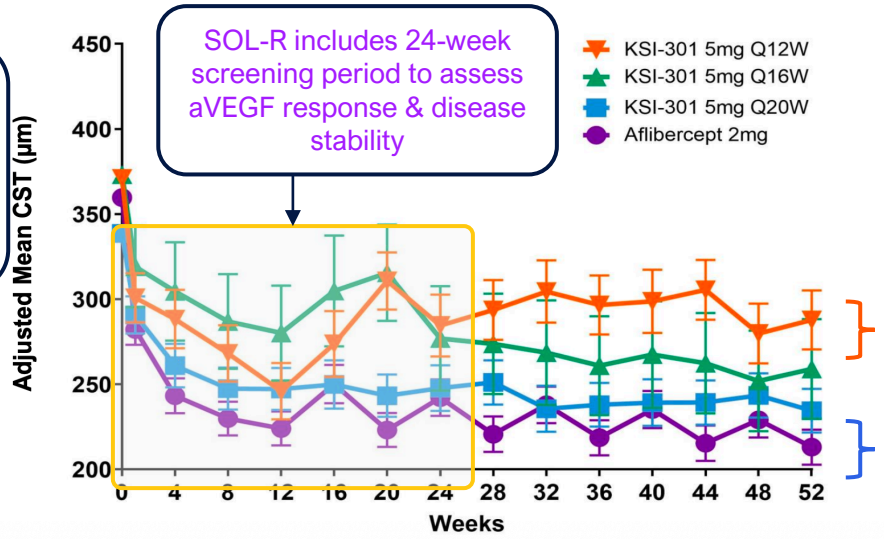
After the loading phase, the initial clinical effect deteriorated in the patients who met criteria for adjustment to the Q12W dosing interval, and subsequent Q12W dosing was insufficient

Proportion of patients in the KSI-301 arm on each treatment interval, among those completing Year 1



Q12W patients likely had early persistent fluid and would be *excluded* from SOL-R

OCT / CST Over Time by Patient Subgroup, among those completing Year 1



Unlikely SOL-R Patient

More likely SOL-R Patient

Least square means and 95% CI are based on MMRM model with treatment, visit, baseline CST, baseline BCVA categories, BCVA-low luminance VA baseline categories, geographical location categories, and treatment (KSI-301 Q20W, Q16W, Q12W, Aflibercept Q8W) by visit interaction.
Q12W: every 12 weeks; Q16W: every 16 weeks; Q20W: every 20 weeks; OCT: optical coherence tomography; CST: central subfield thickness.

14

*Kodiak modified the Zenkuda formulation after initial pivotal trials including DAZZLE. Ongoing pivotal studies of Zenkuda are evaluating the modified formulation.

1. Regillo CD. Presented at: ARVO Annual Meeting; May 3, 2022; Denver, CO.

BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; AMD, age-related macular degeneration; Q20W, every 20 weeks

OCULAR THERAPEUTIX Retina experience redefined™

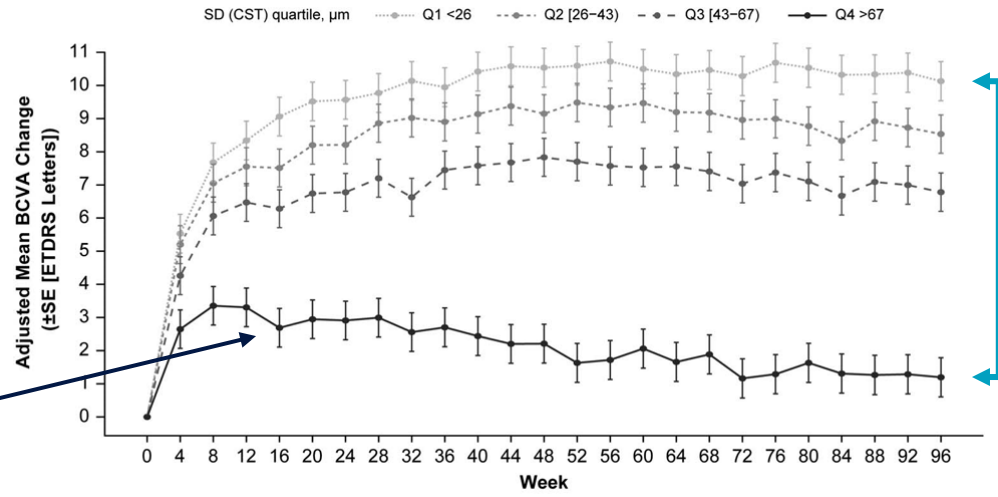
Greater Retinal Thickness Variability During Anti-VEGF Therapy is Associated with Suboptimal Anatomic and Visual Outcomes

Poorer Long-Term Visual Outcomes with Fluctuating Fluid

SOL-R criteria would likely *exclude* patients with most fluid fluctuations *(~25% of tx naïve population)*

EFFECT OF RETINAL THICKNESS VARIABILITY ON VISUAL OUTCOMES AND FLUID PERSISTENCE IN NEOVASCULAR AGE-RELATED MACULAR DEGENERATION

A Post Hoc Analysis of the HAWK and HARRIER Studies



Visual gain ~9 ETDRS letters less in patients with the most fluid fluctuation compared to those with the least

OCULAR THERAPEUTIX Retina experience redefined™

Post hoc, treatment-agnostic analysis of pooled HAWK and HARRIER data from 1752 patients with nAMD treated with brolucizumab or aflibercept. Patients were categorized into quartiles based on the SD of CST measurements from baseline through Week 96, and adjusted BCVA change was evaluated using a repeated measure model.

1. Dugel PU, et al. *Retina*. 2022;42(3):511-518.

ETDRS, Early Treatment Diabetic Retinopathy Study; AMD, age-related macular degeneration; tx, treatment; VEGF, vascular endothelial growth factor

Most Patients in SOL-1 Demonstrated Anatomical Control

SOL-1

Post Hoc Analysis: Patients with Retinal Stability at Week 8

	Wk-8 Wk-4 D1 	Wk-8 Wk-4 D1 
Change in CSFT from Baseline at Week 8	**OTX-TKI 0.45 mg (N=170)**	**Aflibercept 2 mg (N=172)**
≤30 µm increase	114 (67.1%)	126 (73.3%)
>30 µm increase	48 (28.2%)	37 (21.5%)
Missing	8 (4.7%)	9 (5.2%)

OCULAR THERAPEUTIX Retina experience redefined™

Retinal stability defined as central subfield thickness ≤30 micron increase on OCT at Week 8

SOL-1 Learnings for SOL-R: Approximately 30% of Patients Demonstrated Early Persistent Fluid (>30 µm increase at week 8)

Post Hoc Analysis: Patients with Retinal Stability at Week 8

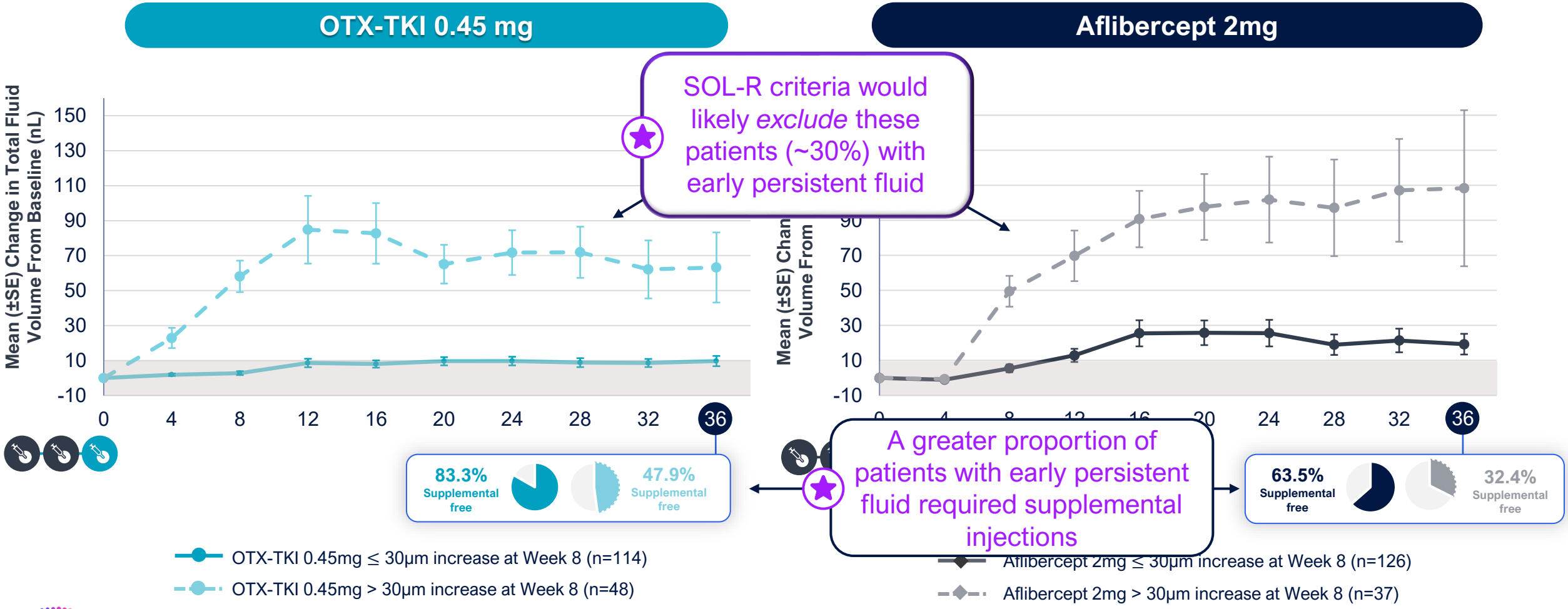
SOL-R criteria would likely *exclude* these patients (~30%) with early persistent fluid

	Wk-8 Wk-4 D1	Wk-8 Wk-4 D1
Change in CSFT from Baseline at Week 8	**OTX-TKI 0.45 mg (N=170)**	**Aflibercept 2 mg (N=172)**
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Retinal stability defined as central subfield thickness ≤30 micron increase on OCT at Week 8.

SOL-1 Learnings for SOL-R: Early Persistent Fluid Patients Had Greater Total Fluid Volume, Fluid Variability, and Supplemental Injections

Post Hoc Analysis: Mean Change From Baseline in Total Retinal Fluid Volume by Week 8 CSFT Subgroup

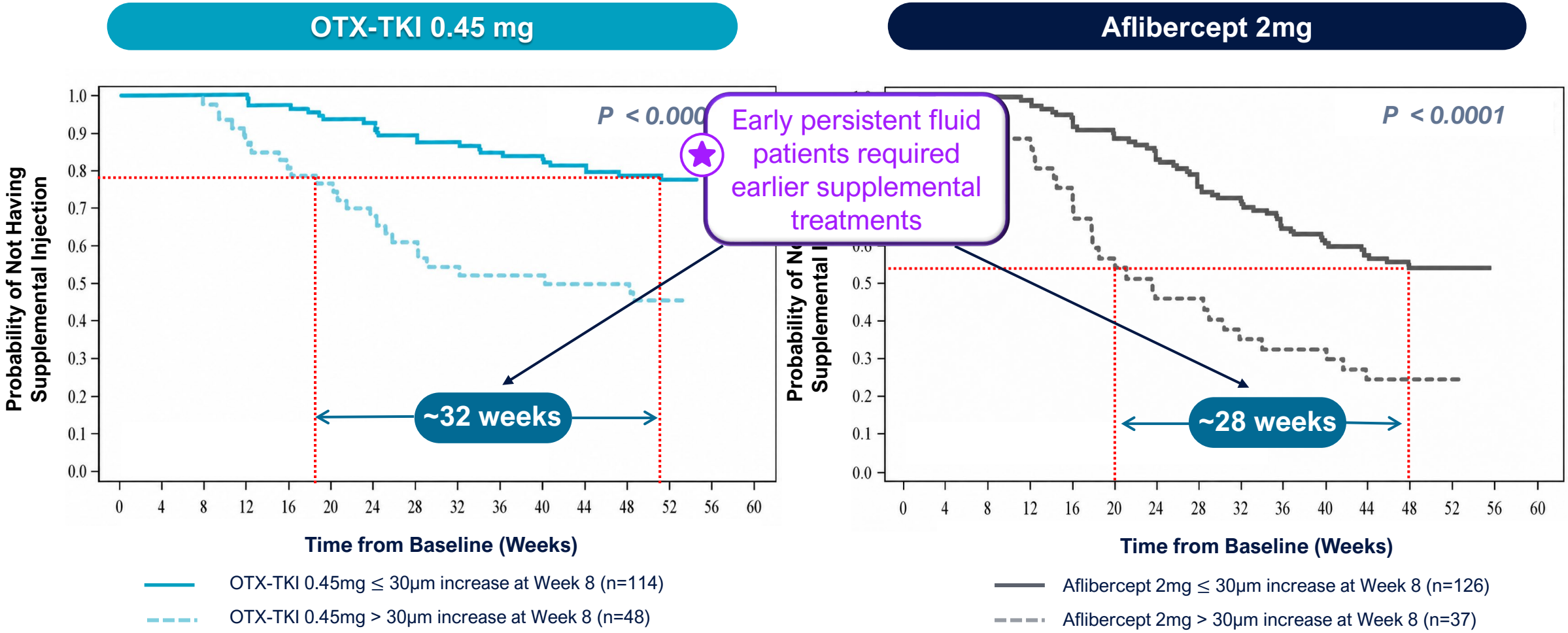


OCULAR THERAPEUTIX Retina experience redefined

Retinal stability defined as central subfield thickness ≤30 micron increase on OCT at Week 8. Analyses were based on observed cases; data were missing for 8 subjects in the OTX-TKI arm and 9 in the aflibercept arm at Week 8. For subjects who received supplemental treatment on or before Week 36, total retinal fluid measurements obtained after the first supplemental injection were treated as missing. Supplemental-free subjects include those who did not require rescue injections as specified by the protocol.
CSFT, central subfield thickness; Suppl, supplemental; OCT, optical coherence tomography

SOL-1 Learnings for SOL-R: Early Persistent Fluid Associated with Significantly Earlier Supplemental Treatment

Post Hoc Analysis: Time to Supplemental Treatment by Retinal Stability at Week 8



OCULAR THERAPEUTIX Retina experience redefined™

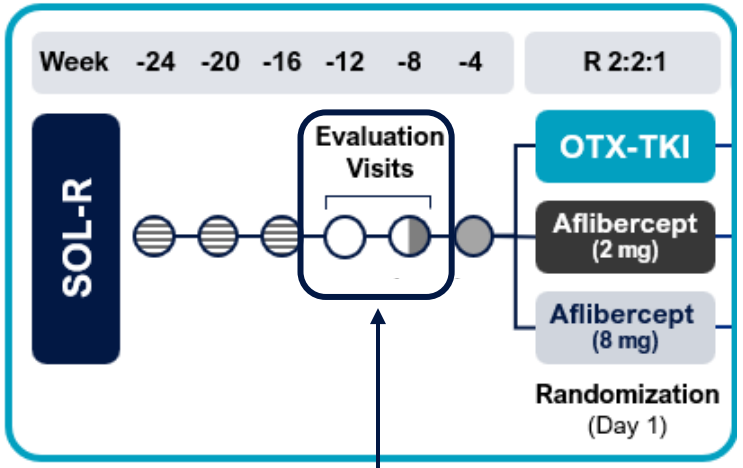
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Core Considerations in nAMD Patient Selection

nAMD Patient Selection

- Early persistent fluid and fluctuations are an indicator of highly variable disease and worse visual outcomes[1,2]
- SOL-R randomized population enriched for stable aVEGF response to increase likelihood of success

SOL-R Screening Period



Two Evaluation Visits

CSFT ≤350 µm at Wk -12 & Wk -8

— AND —

CSFT ≤35 µm increase at Wk -8 from the lowest CSFT at any prior visits

Exclude early persistent fluid and fluid fluctuations from SOL-R

OCULAR THERAPEUTIX Retina experience redefined™

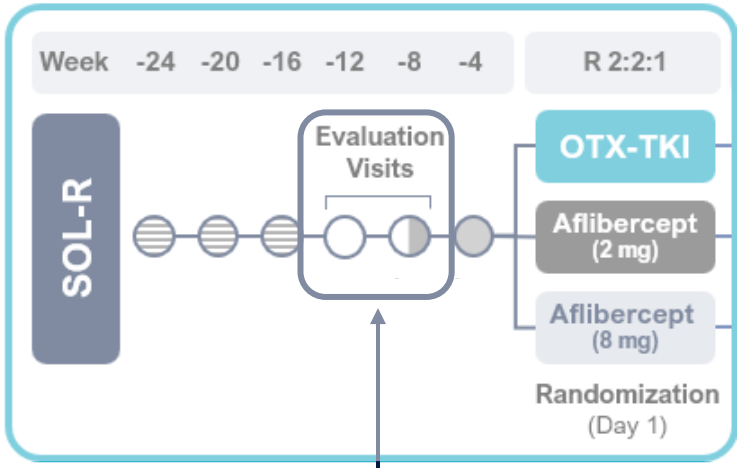
1. Evans RN, et al. *JAMA Ophthalmol*. 2020;138(10):1043-1051; 2. Jaffe GJ, et al. Ophthalmology. 2016;123(9):1856-1864
SF, screen fail; CSFT, central subfield thickness; aVEGF, anti-vascular endothelial growth factor; WK, week

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Exclude early persistent fluid and fluid fluctuations from SOL-R

~20%

Screen fail rate due to early persistent fluid and fluid fluctuations

OCULAR THERAPEUTIX Retina experience redefined™

1. Evans RN, et al. *JAMA Ophthalmol*. 2020;138(10):1043-1051; 2. Jaffe GJ, et al. Ophthalmology. 2016;123(9):1856-1864; 3. Lanzetta P, Korobelnik JF, Heier JS, et al. Intravitreal aflibercept 8 mg in neovascular age-related macular degeneration (PULSAR): 48-week results from a randomised, double-masked, non-inferiority, phase 3 trial. Lancet. 2024;403:1141–1152. doi:10.1016/S0140-6736(24)00063-1. 4. Heier JS, Brown DM, Chong V, et al. Intravitreal aflibercept (VEGF Trap-Eye) in wet age-related macular degeneration. Ophthalmology. 2012;119:2537–2548. doi:10.1016/j.ophtha.2012.09.006.

SF, screen fail; CSFT, central subfield thickness; aVEGF, anti-vascular endothelial growth factor; WK, week

OTX-TKI Phase 3 Clinical Programs

Evaluating the efficacy, durability, and safety of OTX-TKI in nAMD

nAMD

SOL-1

Superiority Trial

Durability of a single OTX-TKI injection

SOL-R

Non-Inferiority Trial

Repeat dosing every 6 months

SOL-X

Open-Label Extension

Long-term safety and disease modifying potential of continuous VEGF suppression*

OCULAR THERAPEUTIX Retina experience redefined™

nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor

*Eligible patients who complete end of Year 2 visit in SOL-1 or SOL-R

SOL-X: Unlocking Long-Term Value with OTX-TKI

Designed to evaluate safety and disease modifying potential of OTX-TKI

Primary Trials

Initial Treatment Arms

SOL-1

- OTX-TKI
- Aflibercept (2 mg)

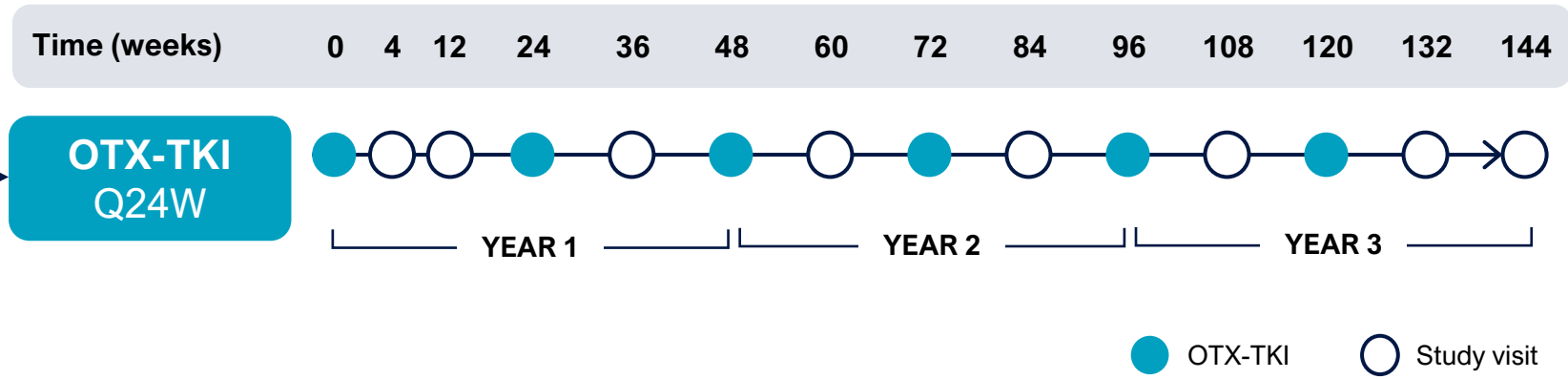
SOL-R

- OTX-TKI
- Aflibercept (2 mg)
- Aflibercept (8 mg)

SOL-X

Three-year additional follow-up

OTX-TKI Q24W



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ClinicalTrials.gov Identifier: NCT07516132

Q24W, every 24 weeks

HELIOS: OTX-TKI Diabetic Retinopathy Clinical Program

Evaluating the efficacy, durability and safety of OTX-TKI in DR

HELIOS

NPDR

HELIOS-1

Phase 1 Safety Trial

Safety and efficacy of a single OTX-TKI hydrogel in moderately-severe to severe NPDR without CI-DME

REGISTRATIONAL TRIAL

HELIOS-3

Phase 3 Superiority Trial

48-week dosing intervals in moderately-severe to severe NPDR without CI-DME

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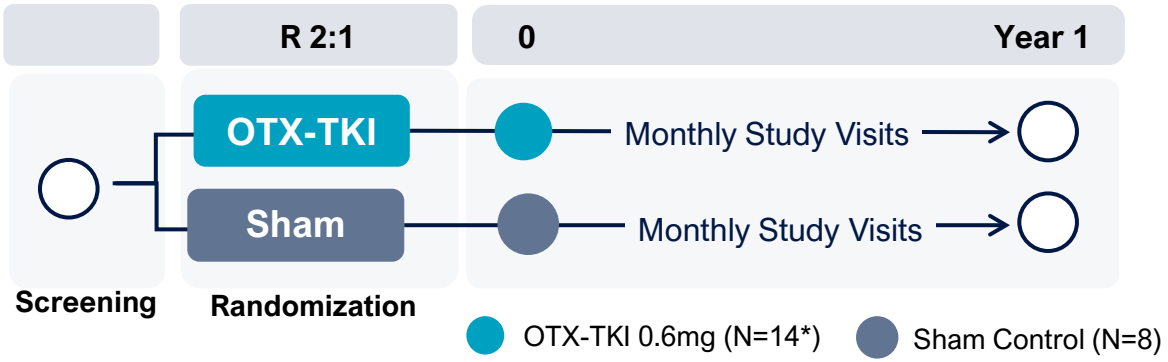
1. Data on File 059. Ocular Therapeutix. 2. Data on File 032. Ocular Therapeutix.
CI-DME, center-involved diabetic macular edema; DR, diabetic retinopathy; NPDR, nonproliferative diabetic retinopathy;

HELIOS-1 Study of OTX-TKI in NPDR

HELIOS-1

Design

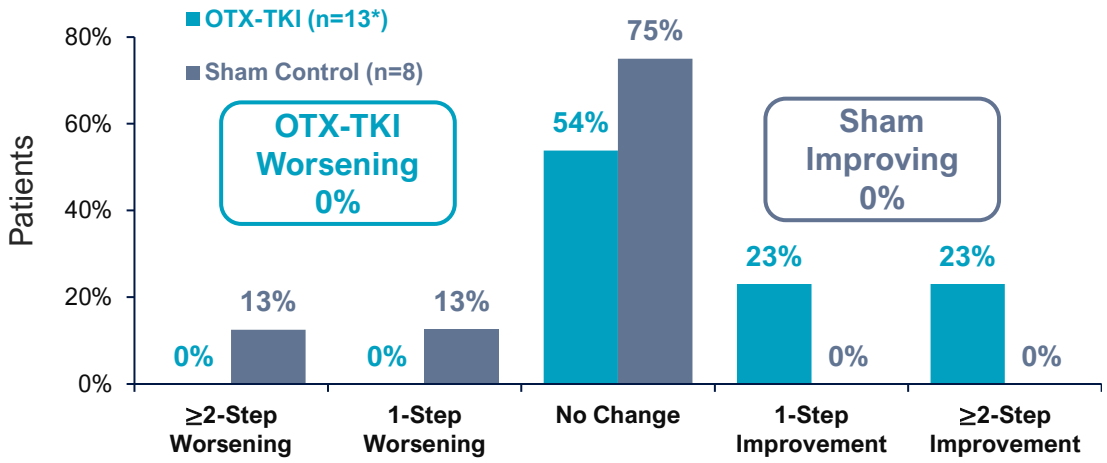
Multi-center, double-masked, randomized, parallel group study of OTX-TKI in moderately-severe to severe NPDR without CI-DME



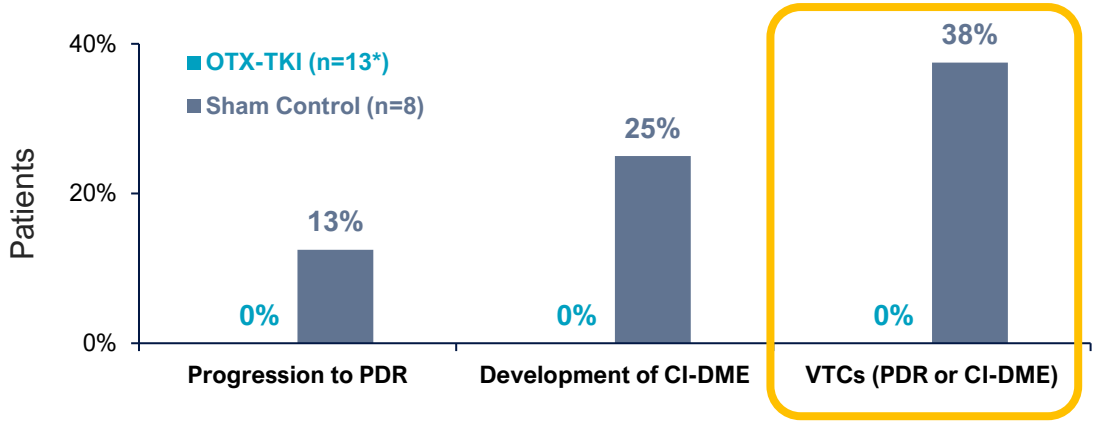
Safety

- In the OTX-TKI arm, all ocular AEs in the study eye were mild
- 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 supplemental injections

Change in DRSS from Baseline to Week 48[1]



Progression to VTCs at Week 48[2]



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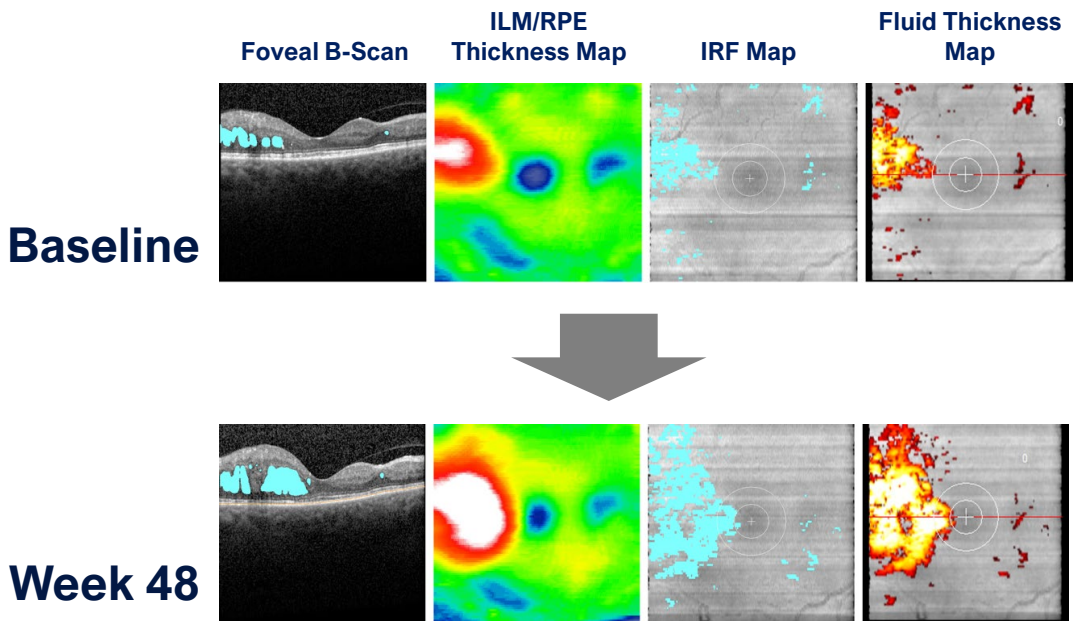
*14 subjects enrolled in OTX-TKI treatment arm, with one subject death unrelated to treatment.
DRSS, diabetic retinopathy severity scale; NPDR, non-proliferative diabetic retinopathy; CI-DME, center-involved diabetic macular edema; PDR, proliferative diabetic retinopathy; VTC, vision-threatening complication

HELIOS-1: DME Cases with AI-based Retinal Fluid Analysis

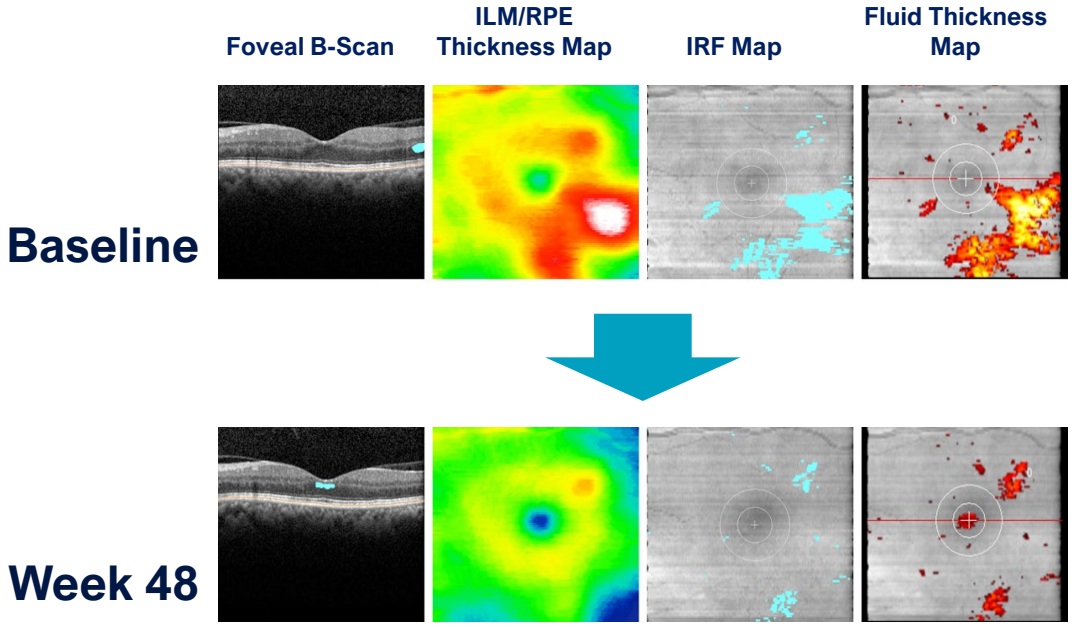
HELIOS-1

HELIOS

SHAM CONTROL



OTX-TKI



Case study of one patient. Individual results may vary.

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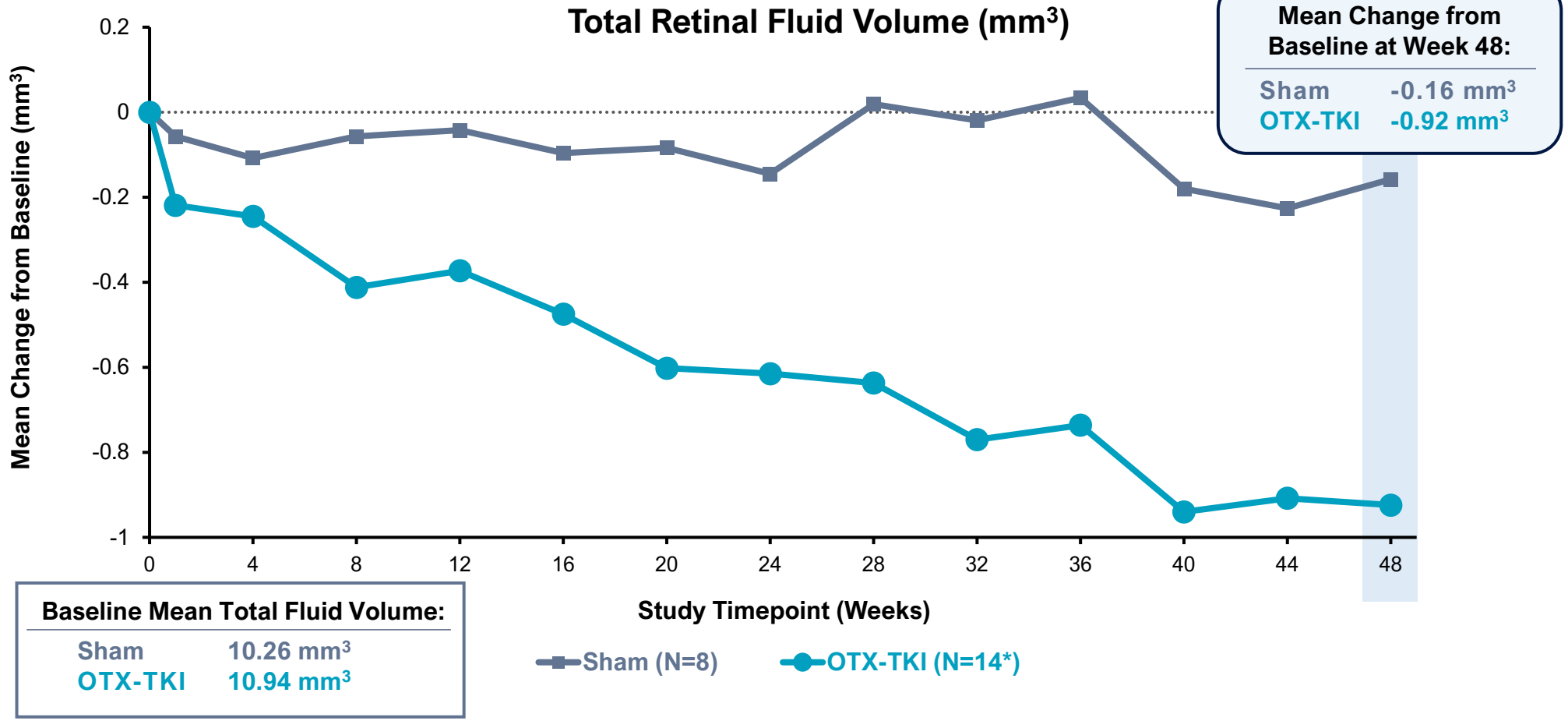
DME (diabetic macular edema); OCT (optical coherence tomography); ; non-CI-DME (non-center-involved diabetic macular edema)

Ehlers J, et al. Longitudinal Quantitative Ultra-widefield Retinal Leakage Assessment and Macular Volumetric Fluid Outcomes Following a Single Axitinib Hydrogel (OTX-TKI) in the HELIOS Trial for Non-proliferative Diabetic Retinopathy. Presented at Retina Society. Chicago, IL. September 11, 2025.

OTX-TKI Subjects Consistently Had Greater Reductions from Baseline in AI-based Total Retinal Volume Compared to Sham

HELIOS-1

Post Hoc Analysis



Mean Change from Baseline at Week 48:

Sham	-0.16 mm³
OTX-TKI	-0.92 mm³

Baseline Mean Total Fluid Volume:

Sham	10.26 mm³
OTX-TKI	10.94 mm³

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

Danzig C, et al. Volumetric Macular Fluid Analysis of the Impact of a Single Axitinib Intravitreal Injection (OTX-TKI) from the HELIOS Clinical Trial for Diabetic Retinopathy. Presented at Retina World Congress. Fort Lauderdale, FL. May 10, 2025.

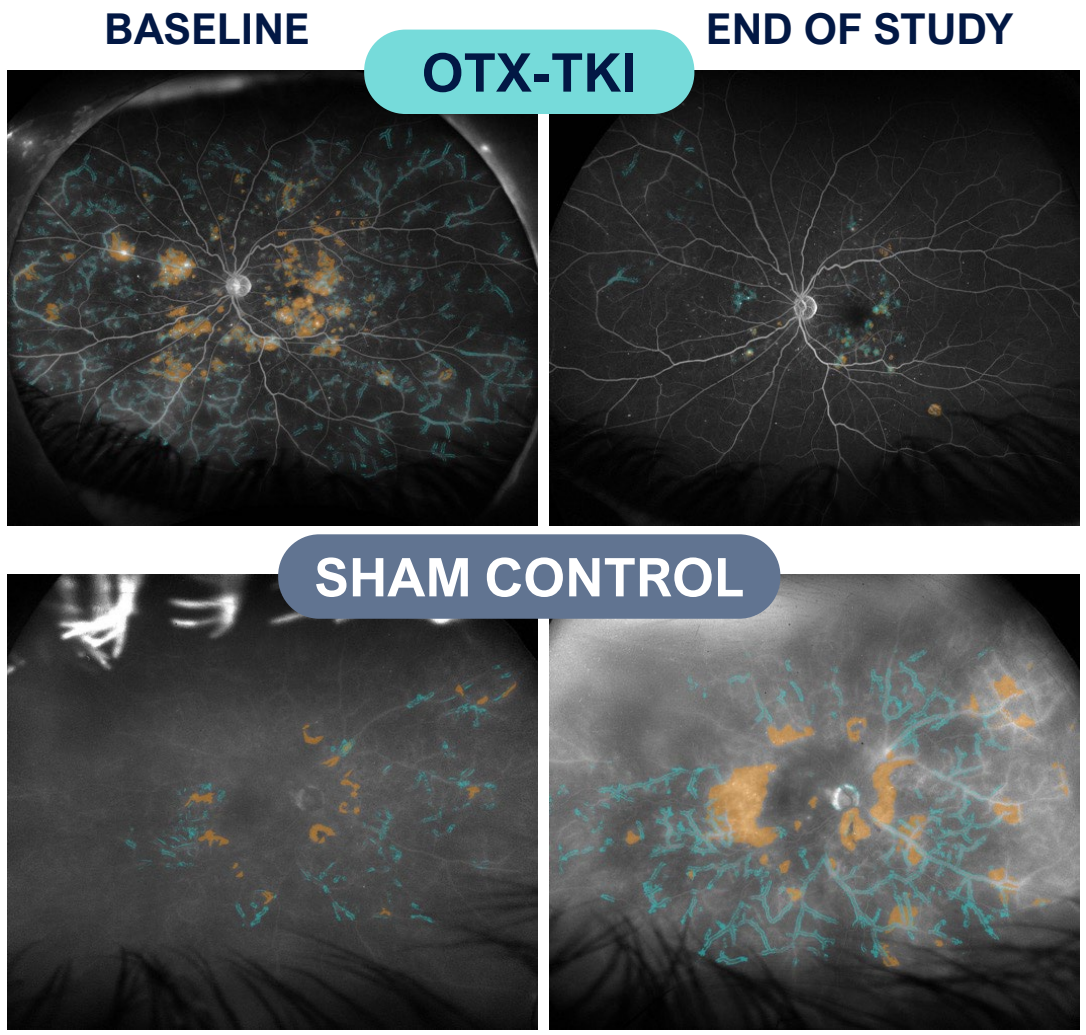
HELIOS-1: Total Retinal Vascular Leakage

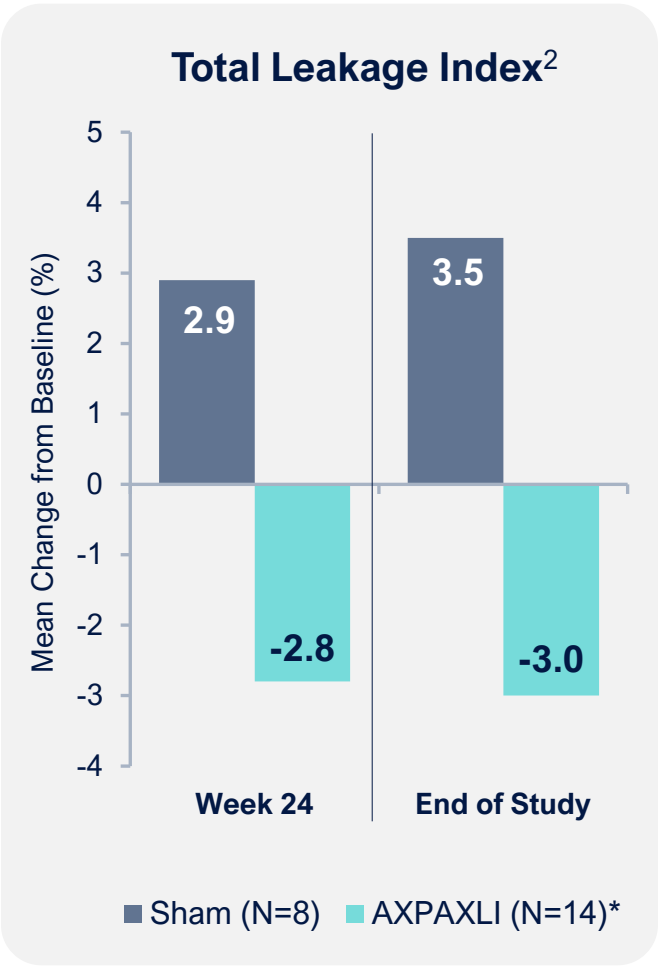
HELIOS-1

Post Hoc Analysis

Higher levels of total retinal vascular leakage associated with[1]:

- More advanced DR
- Greater risk of disease progression
- Worse visual outcomes





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

DR (diabetic retinopathy)

1. Writing Committee for the DRCR Retina Network, et al. *Ophthalmol Retina*. 2025;9(3):243-252. 2. Figures from Ehlers J, et al. Volumetric Macular Fluid Analysis of the Impact of a Single Axitinib Intravitreal Implant (OTX-TKI) from the HELIOS Clinical Trial for Diabetic Retinopathy. Presented at Angiogenesis. Virtual. February 8, 2025.

Diabetic Retinopathy Program

HELIOS-3 Study Design

HELIOS-3

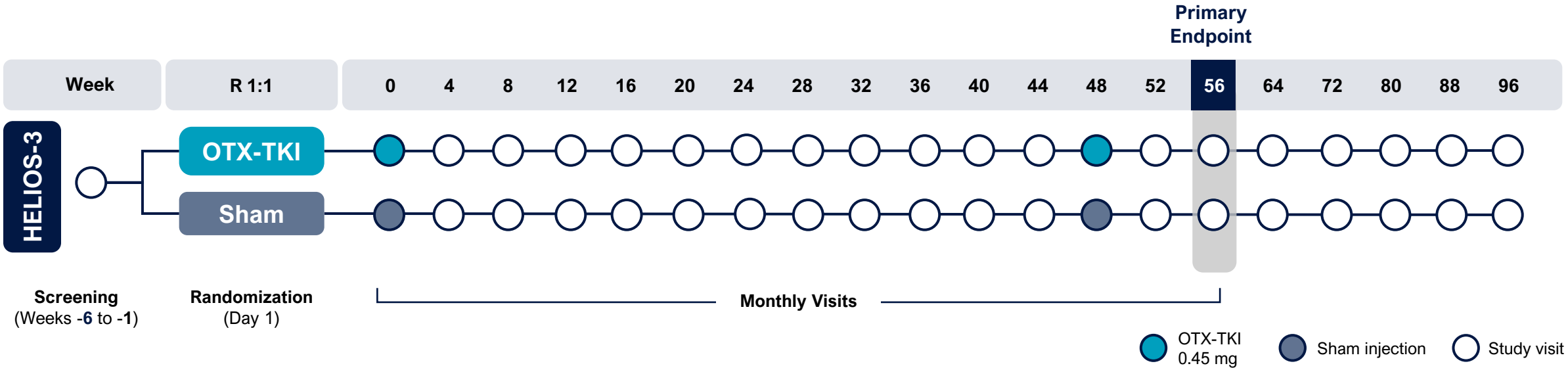
Evaluation of only Q12M OTX-TKI regimen vs Sham

Design

Superiority study of OTX-TKI in **~620** subjects with moderately-severe to severe NPDR without CI-DME

Primary Endpoint (Week 56)

Ordinal DRSS 2-step change status at **Week 56** from baseline
(≥ 2 step improvement, ≥ 2-step worsening, < 2-step change in either direction)



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ClinicalTrials.gov Identifier: NCT07235085

CI-DME, center-involved diabetic macular edema; DR, diabetic retinopathy; DRSS, Diabetic Retinopathy Severity Scale; mg, milligram; NPDR, nonproliferative diabetic retinopathy; OTX-TKI, axitinib intravitreal hydrogel; Q12M, every 12 months; R, randomization; TKI, tyrosine kinase inhibitor; vs, versus.

OTX-TKI Development Program Summary

OTX-TKI

OTX-TKI demonstrated superior maintenance of vision* to aflibercept 2 mg at Week 36 in nAMD



nAMD Program

PHASE 3

Superiority Trial

Durability of a single OTX-TKI injection

Primary endpoint met

SOL-1

PHASE 3

Non-Inferiority Trial

Repeat dosing every 6 months

Randomization complete - topline data expected in Q1 ‘28

SOL-R

DR Program

PHASE 3

Superiority Trial

Evaluating yearly dosing

Enrollment in HELIOS-3 is underway

HELIOS-3

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*Maintenance of vision defined as proportion of subjects who maintain visual acuity, a loss of <15 ETDRS letters of BCVA from baseline.
DR, diabetic retinopathy; nAMD, neovascular age-related macular degeneration

Redefining the Management of nAMD

The Impact of Durability and Sustained Disease Control

November 7, 2026

OSN New York | New York, NY

OCULAR THERAPEUTIX

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Panel Discussion



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MD, FASRS (Moderator)

Founder and Director of Clinical Research, Retina Macula Institute of Arizona,
Scottsdale, AZ



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MD, MBA, FASRS

Vice Chair, Clinical Affairs, Department of Ophthalmology, Keck School of Medicine,
Los Angeles, CA



Dilsher S. Dhoot
MD, FASRS

Adjunct Clinical Assistant Professor at Keck School of Medicine, University of Southern California and Vitreoretinal Specialist at California Retina Consultants
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