Redefining the Management of nAMD

The Impact of Durability and Sustained Disease Control

July 16, 2026

American Society of Retina Specialists | Montreal, Canada

OCULAR THERAPEUTIX

Retina experience redefined™

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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

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- **Speaker:** Alcon, ANI Pharmaceuticals, Apellis, Astellas, Genentech, Regeneron,
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- **Research support**: AbbVie/Allergan, Adverum, AGTC, Alcon Laboratories, Inc., Aldeyra, Apellis, Gyroscope, Heidelberg Engineering, Janssen/Johnson & Johnson, National Eye Institute, Novartis, Ocugen Inc., Ocular Therapeutix, Optos, REGENXBIO, Roche/GenentechStock
- **Stock/Stock options:** Lexitas, Ocugen Inc.
- **Patents/Royalty**: Alcon Laboratories, Inc.

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Agenda

Background
Mark R. Barakat, MD

Science Behind the Therapy
Lejla Vajzovic, MD

SOL-1 Results
Dilsher S. Dhoot, MD

SOL-1: Clinical Evidence
Lejla Vajzovic, MD

Key Insights
Mark R. Barakat, MD

Clinical Program Update
Arshad M. Khanani, MD

Panel Discussion
Moderator: Arshad M. Khanani, MD

Background

Mark R. Barakat, MD

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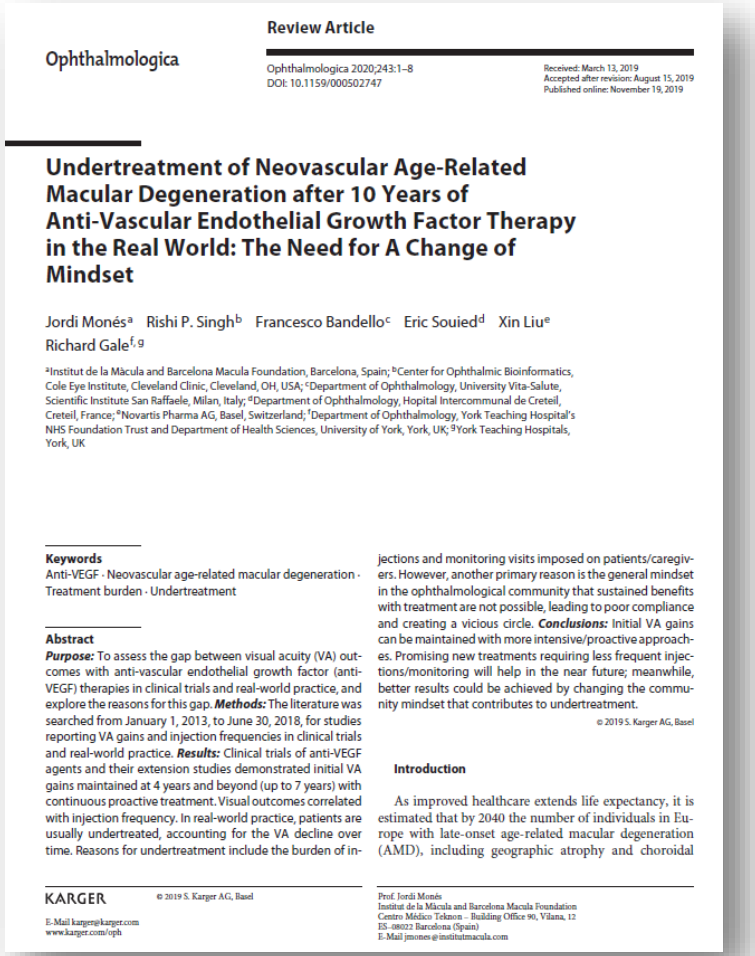
1. MacCumber MW, et al. *Can J Ophthalmol*. 2023;58(3):252-261. 2. Ophthalmic Market Trends: Quarterly US Retina Edition: Q3-2024 Analysis of Historical Trends and Latest Developments. Market Scope; 2024. 3. Varano M, et al. *Clin Ophthalmol.* 2016;10:257-267. 4. Khanani AM, et al. *Ophthalmology Retina*.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

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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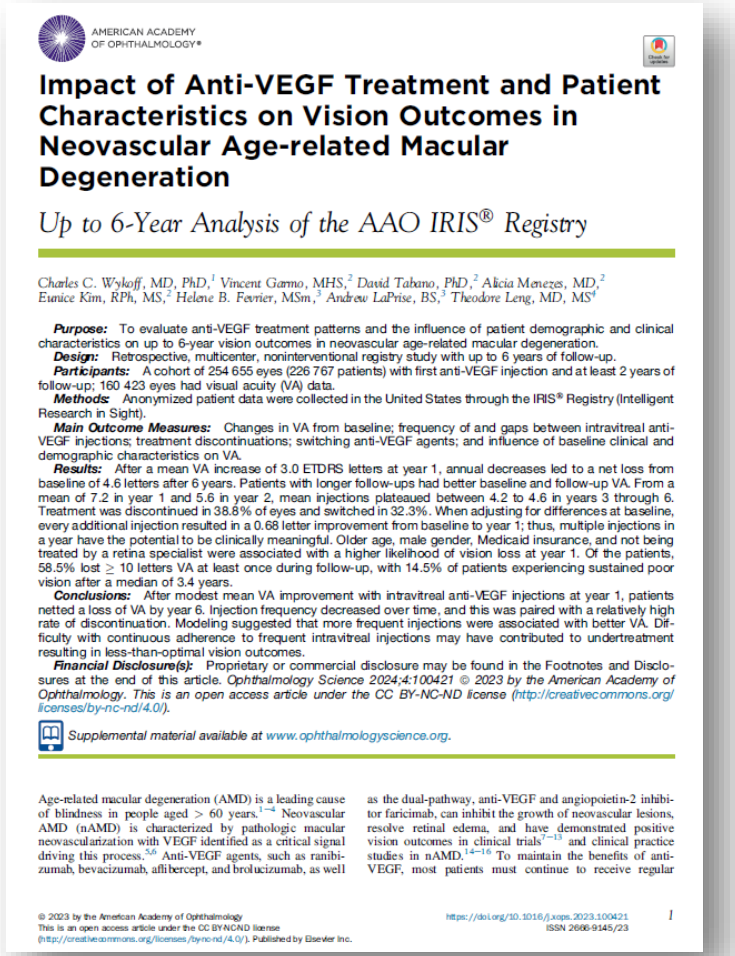

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Impact of Anti-VEGF Treatment and Patient Characteristics on Vision Outcomes in Neovascular Age-related Macular Degeneration

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

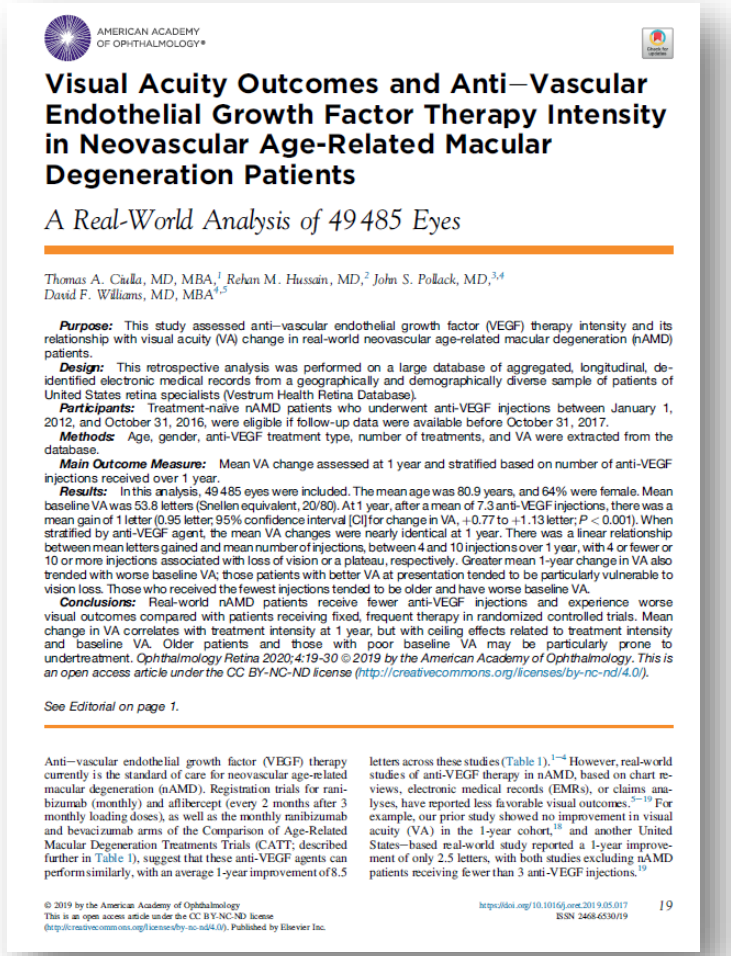
Charles C. Wykoff, MD, PhD,[1] Vincent Garmo, MHS,[2] David Tabano, PhD,[2] Alicia Menezes, MD,[2] Eunice Kim, RPh, MS,[2] Helene B. Fevrier, MSm,[3] Andrew LaPrise, BS,[3] Theodore Leng, MD, MS[4]

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

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]

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

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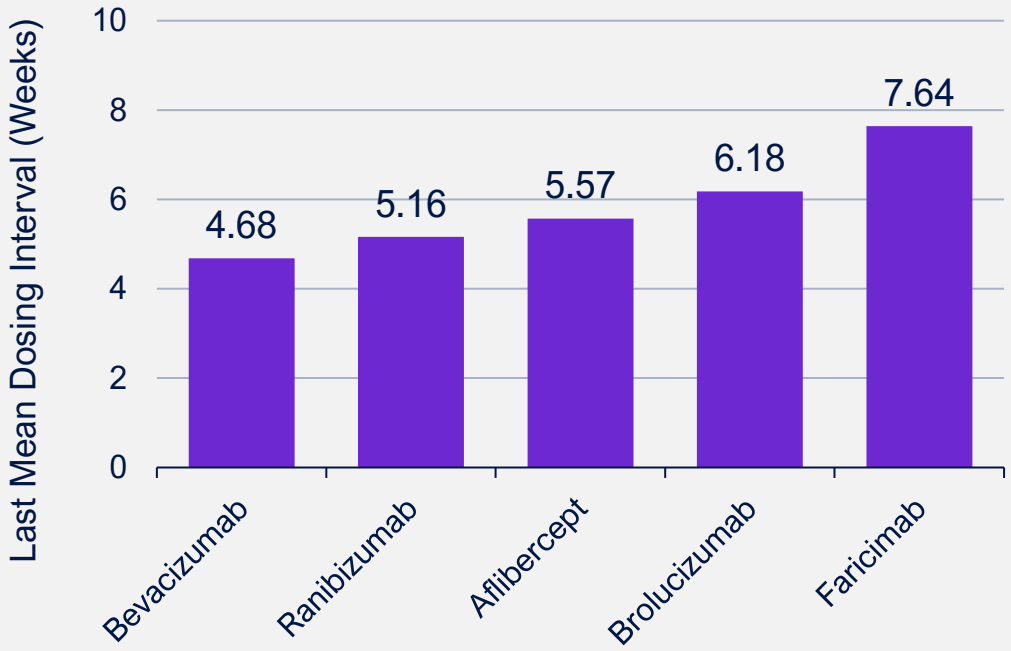
1. Monés J, et al. *Ophthalmologica*. 2020;243(1):1-8. 2. Wykoff CC, et al. *Ophthalmol Sci*. 2023;4(2):100421. 3. Ciulla TA, et al. *Ophthalmol Retina*. 2020;4(1):19–30.

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

*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

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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**

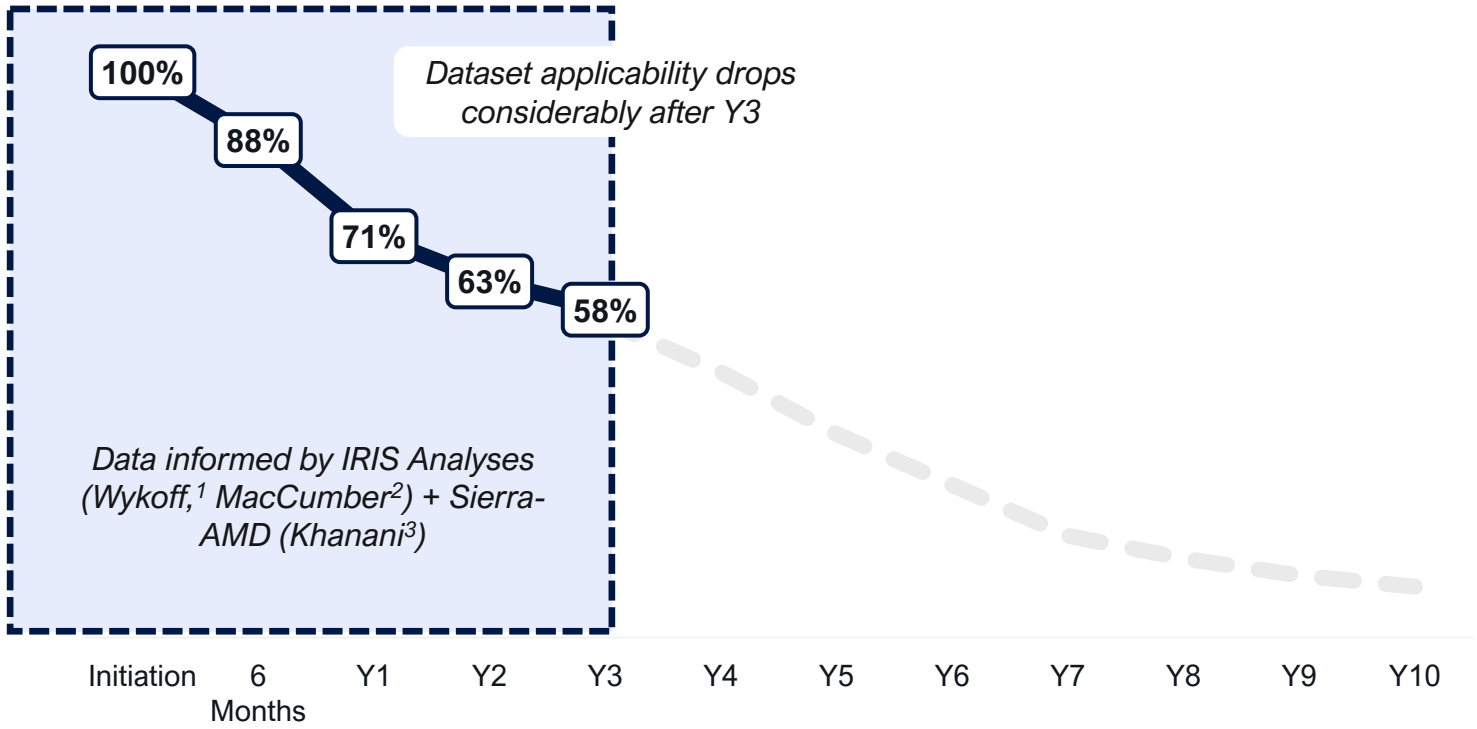
Limited Longer-Term Follow-Up

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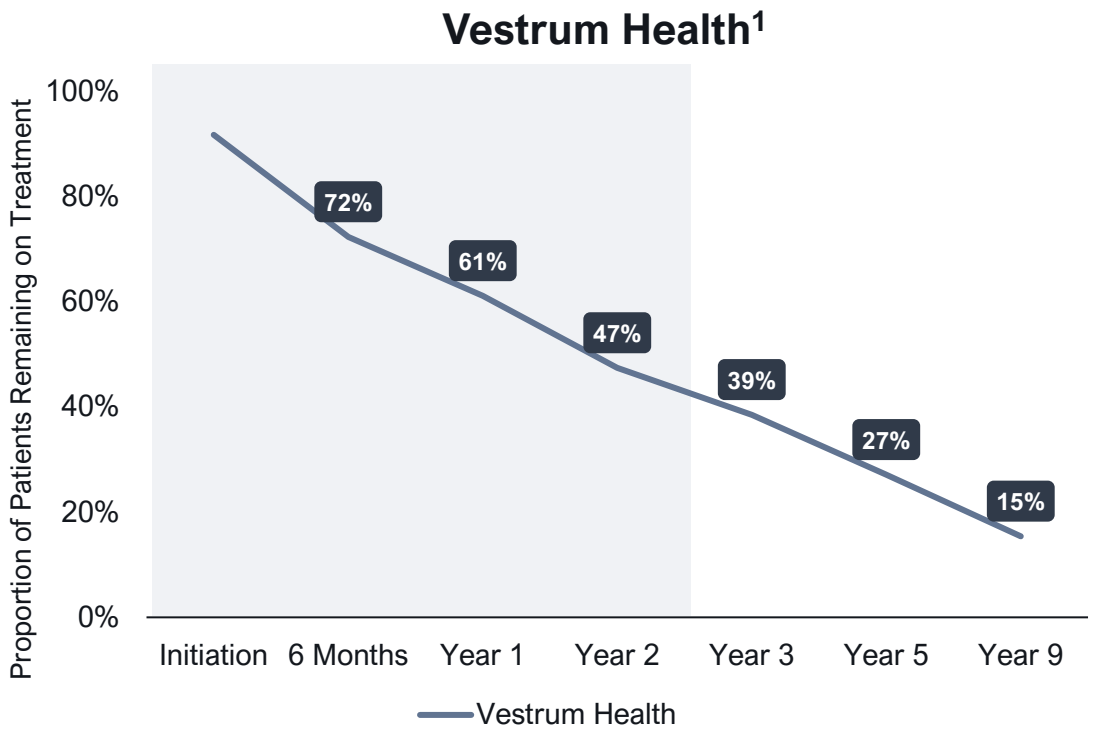
*Literature-Based Attrition Curve generated by Ocular Therapeutix by analysis of references 1-3. Trend line following Year 3 is illustrative and based on decline shown in in Years 1-3

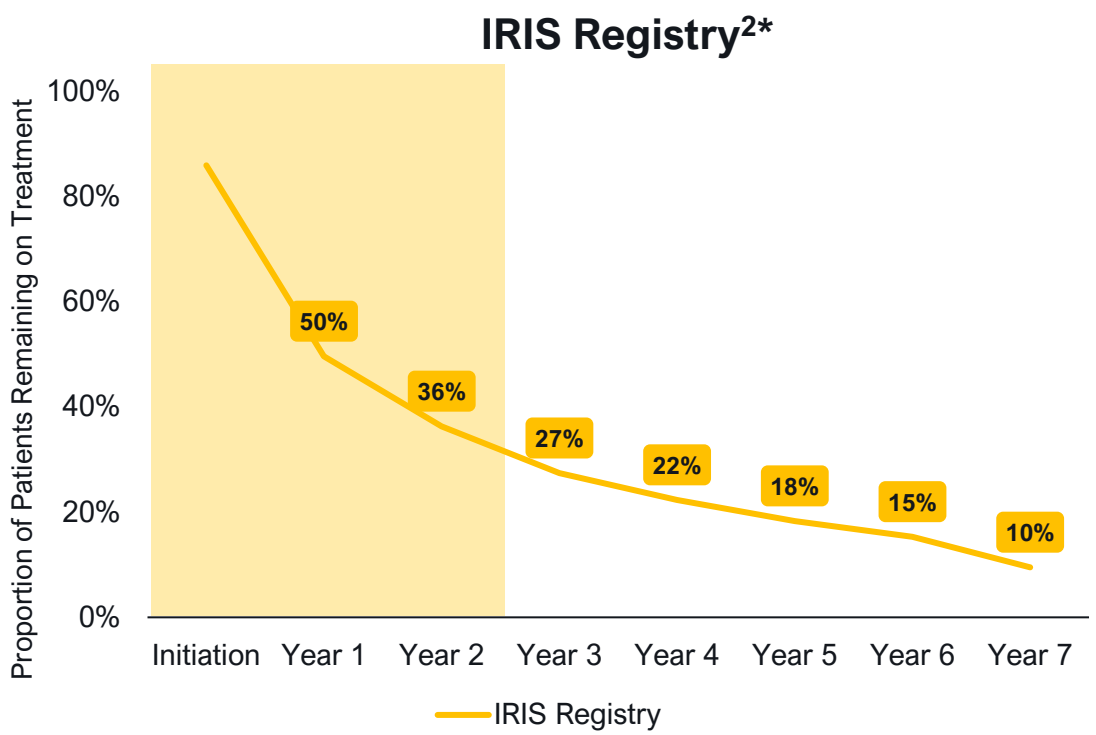
1. Wykoff CC, et al. *Ophthalmol Sci*. 2023;4(2):100421. 2. MacCumber MW, et al. *Can J Ophthalmol*. 2023;58(3):252-261. 3. Khanani AM, et al. *Ophthalmol Retina*. 2020;4(2):122-133.

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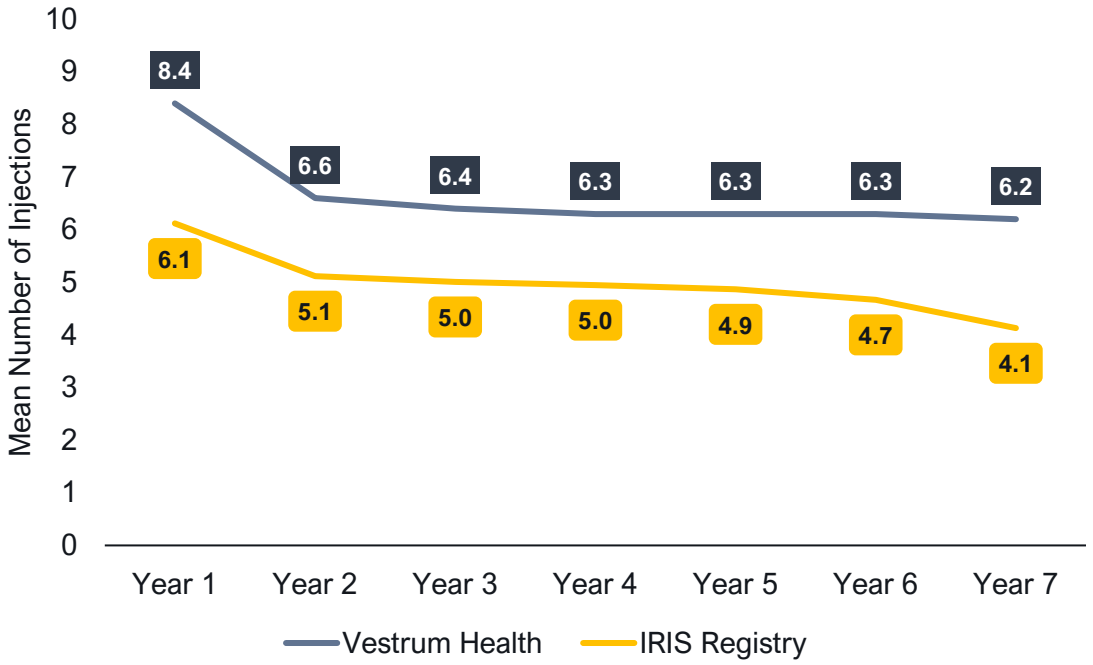
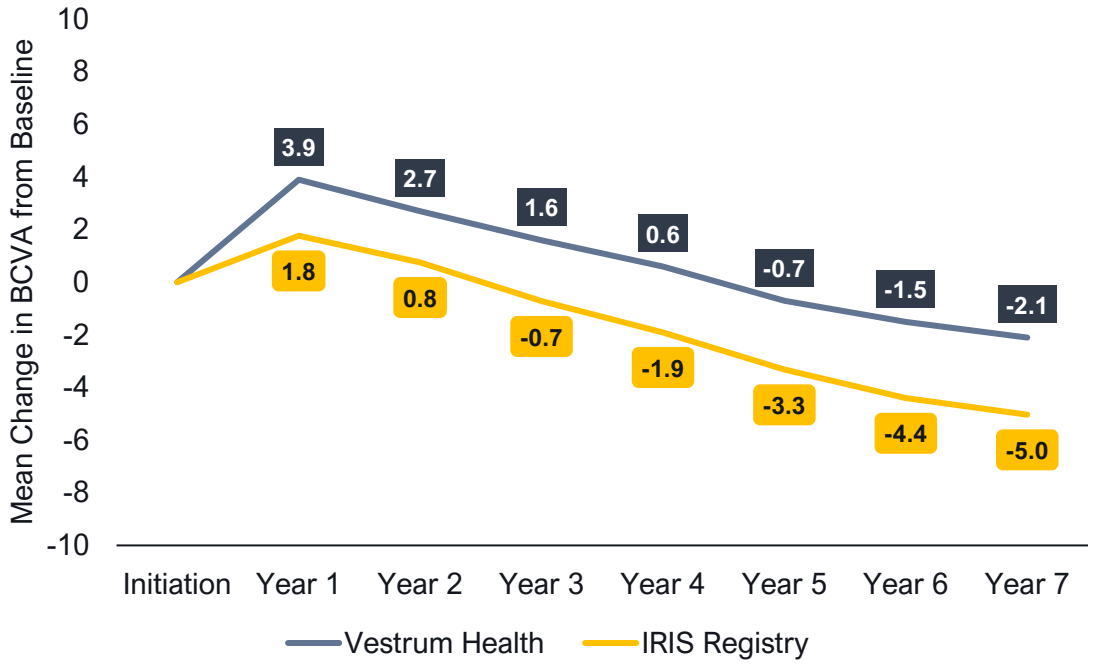
*Cohort with the longest observation period for IRIS Registry with 67,156 eyes
Time to discontinuation was defined as > 6 months without anti-VEGF
1. Data on File 048. Ocular Therapeutix. 2026. 2. Data on File 047. Ocular Therapeutix. 2026.
IRIS, Intelligent Research in Sight

Real-World Anti-VEGF Use Shows Fewer Injections Over Time, Driving Gradual Vision Decline

Injection Frequency[1,2]



Long-Term Visual Outcomes[1,2*]



Injection Frequency Declines Over Time in Both Databases
Vestrum Health drops from 8.4 at Year 1 to 6.2 by Year 7
IRIS Registry drops from 6.1 at Year 1 to 4.1 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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*Visual outcomes: mean change from baseline in ETDRS letters
1. Data on File 48, Ocular Therapeutix. 2026. 2. Data on File 047. Ocular Therapeutix. 2026
VEGF, vascular endothelial growth factor; IRIS, Intelligent Research in Sight

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

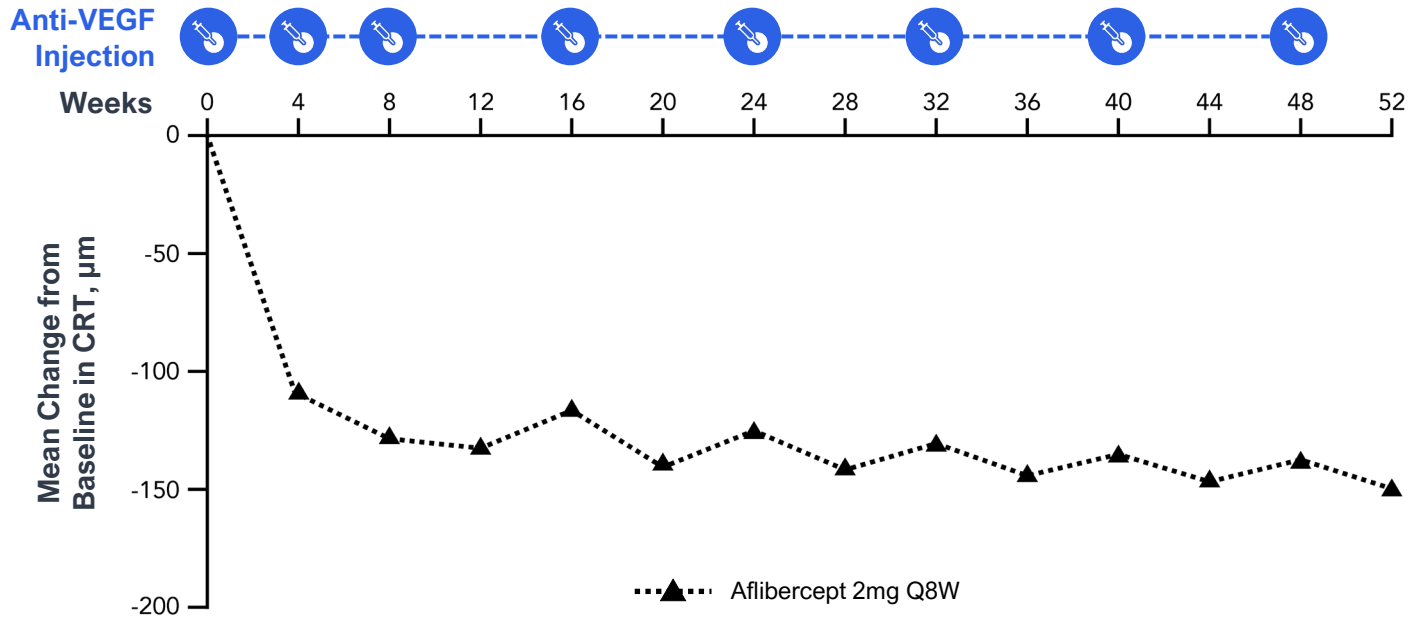


Figure adapted from Heier JS, et al. *Ophthalmology*. 2012;119(12):2537-2548.
VIEW 1 and VIEW 2 were similarly designed, randomized, double-masked, active-controlled Phase 3 trials in patients with nAMD (N=2419) comparing aflibercept dosing regimens with ranibizumab Q4W; figure illustrates mean CRT change 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

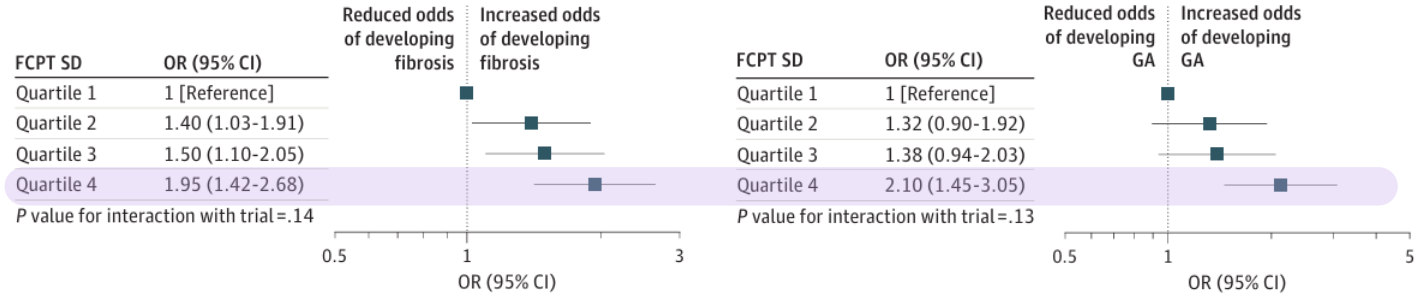
Retinal Thickness Fluctuations

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



Highest retinal thickness variability had approximately **double the odds** of developing fibrosis/macular atrophy

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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

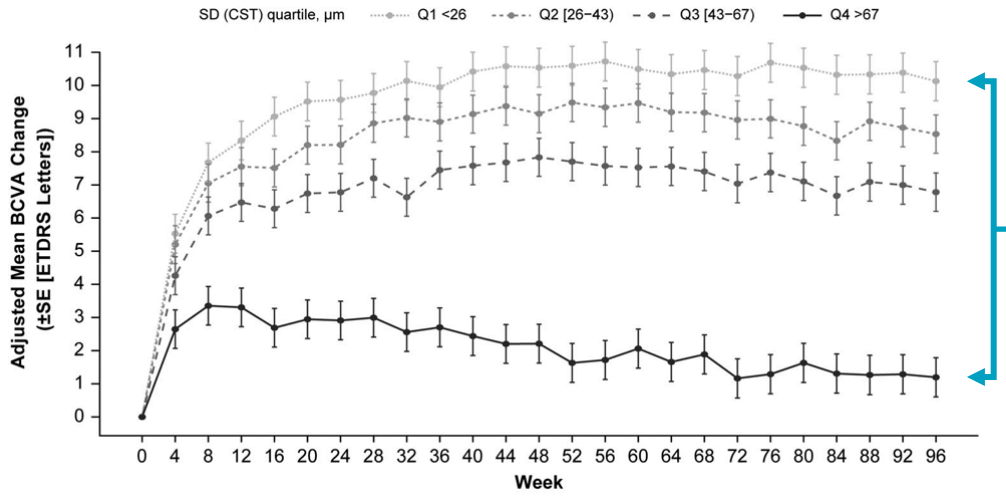
Retinal Thickness Fluctuations

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



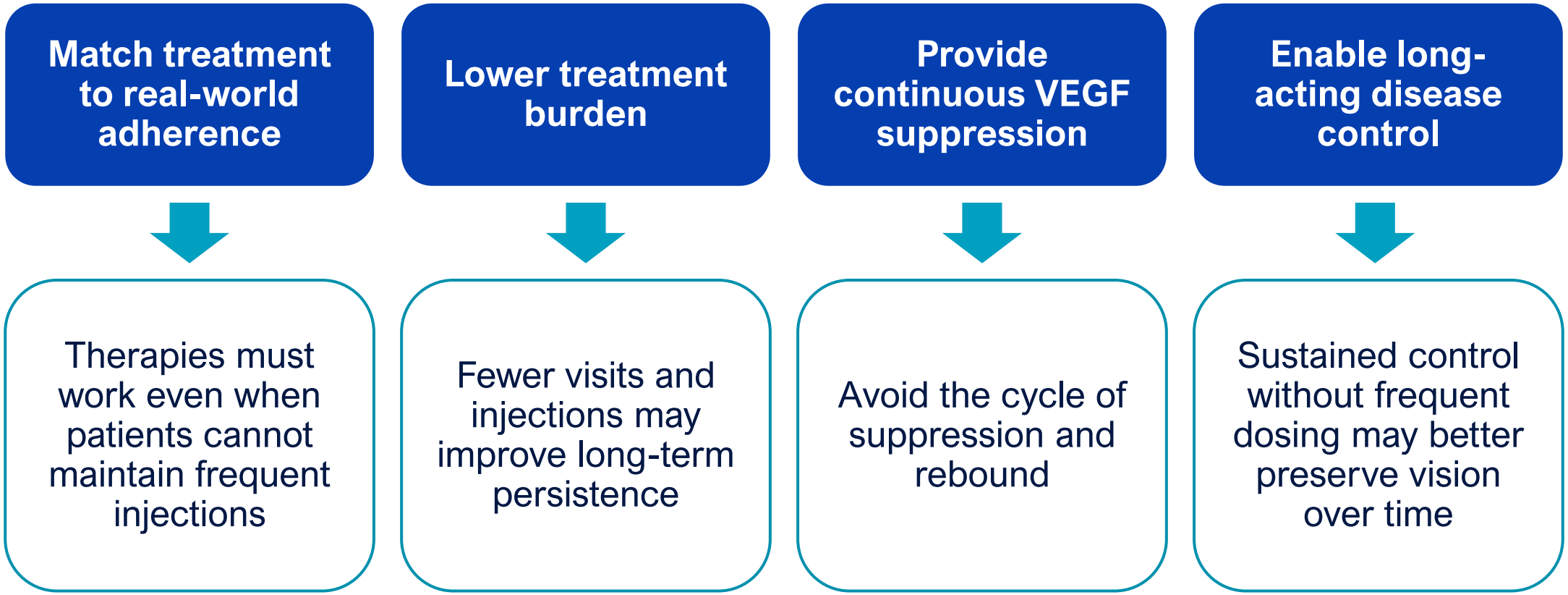
Vision deteriorates by ~9 letters between patients with most and least stable retinal thicknesses

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?



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

Science Behind the Therapy

Lejla Vajzovic, MD

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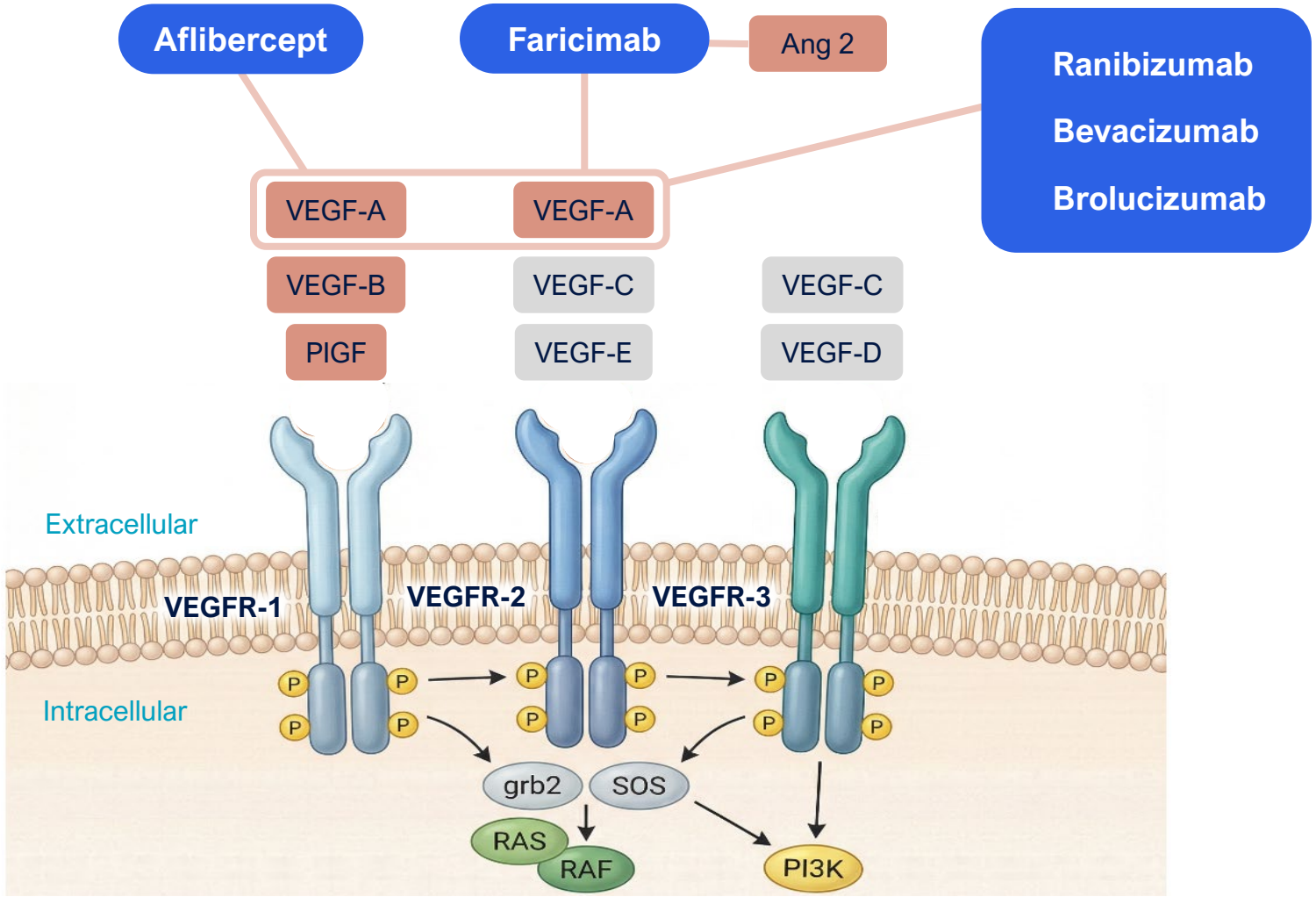
Current Anti-VEGF Therapies Selectively Target Only Extracellular VEGF

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]

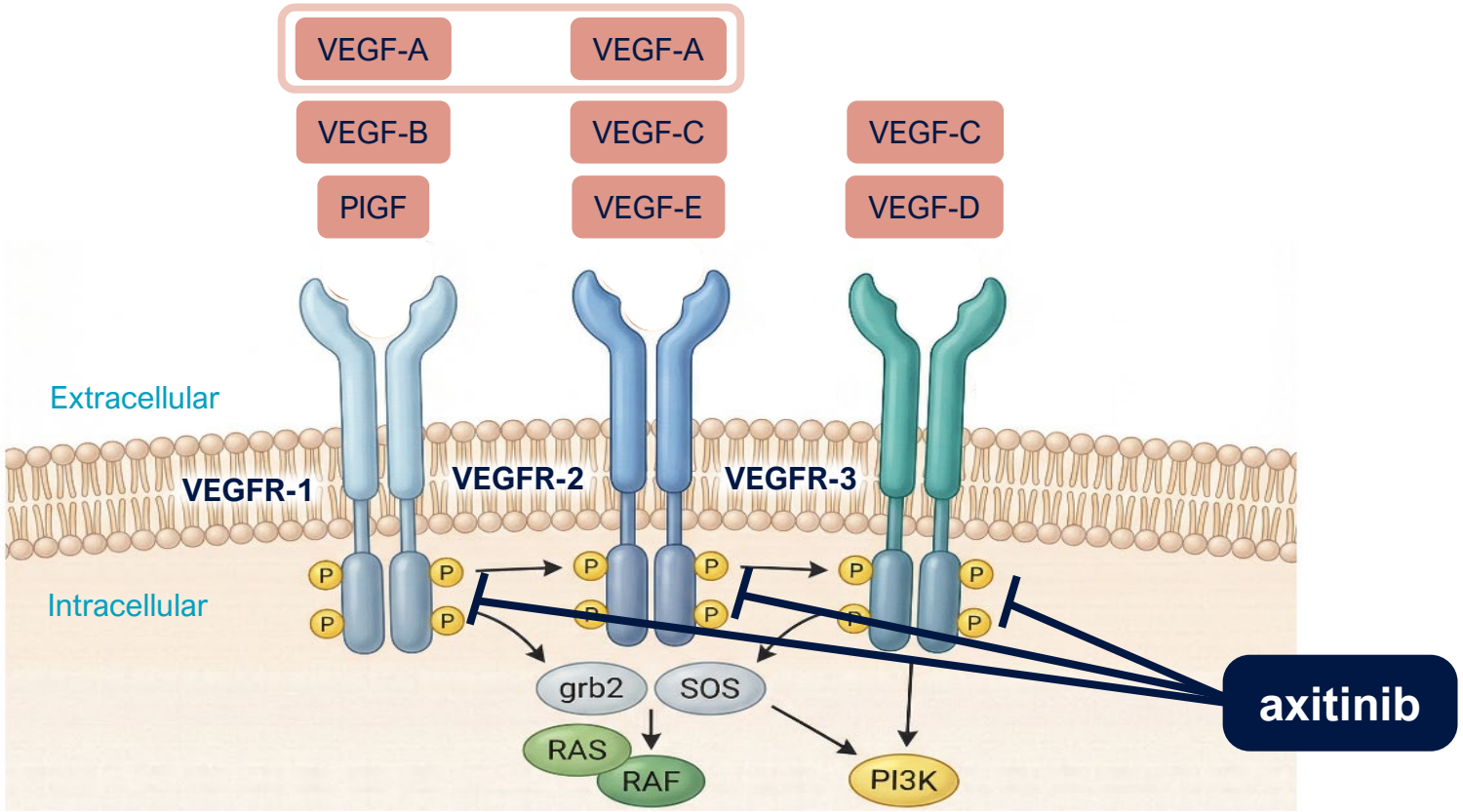
OCULAR THERAPEUTIX Retina experience redefined™

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]

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.

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

AXITINIB

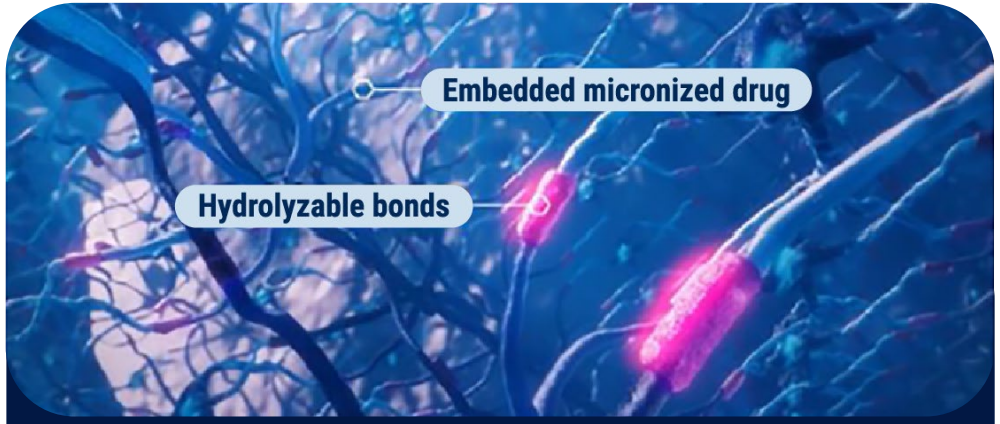
Multi-target Tyrosine Kinase Inhibitor (TKI)

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]

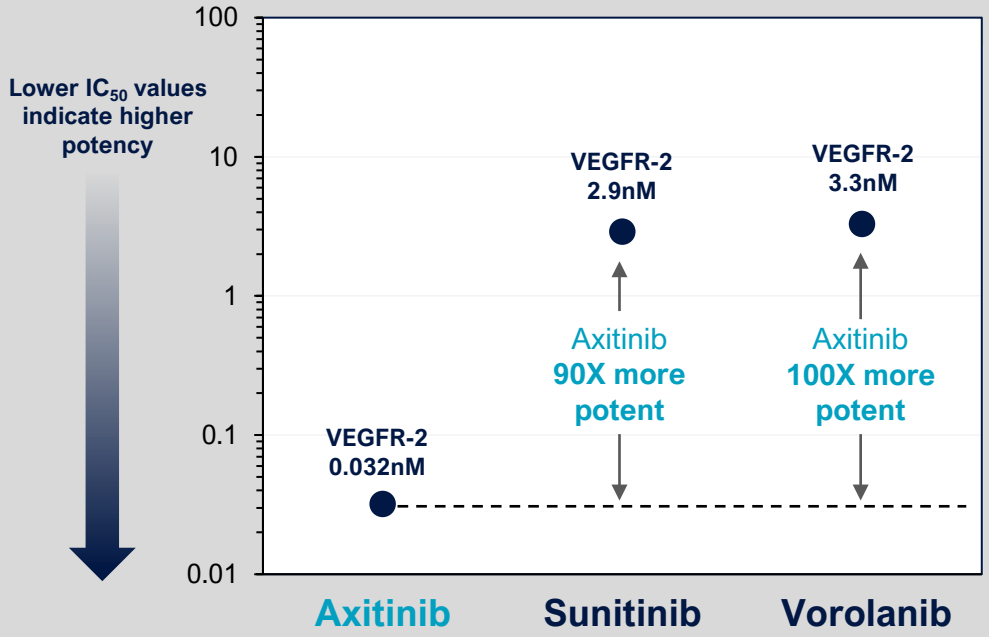
OTX-TKI is an investigational product candidate which has not been approved by the FDA or any regulatory authority.

OCULAR THERAPEUTIX Retina experience redefined™

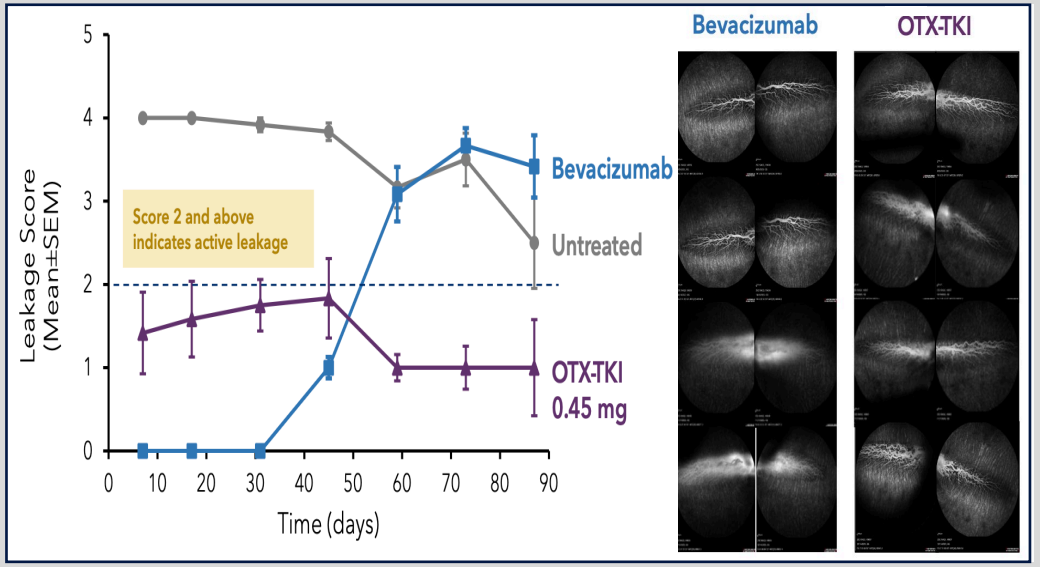
1. Zhao Y, et al. *Oncologist.* 2015;20(6):660-673. 2. Gross-Goupil M, et al. *Clin Med Insights Oncol.* 2013;7:269-277. 3. Blizzard CD, et al. Ocular Implant Containing a Tyrosine Kinase Inhibitor. US Patent 11,439,592 B2. September 13, 2022. 4. Tan CS, et al. *Clin Ophthalmol*. 2022;16:917-933. 5.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

Axitinib: Highly Selective, Very Potent VEGFR Inhibitor

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



VEGF Challenge Rabbit Model[2]



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

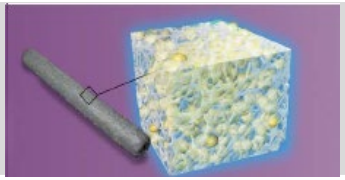
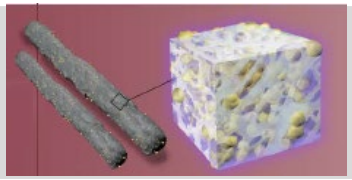
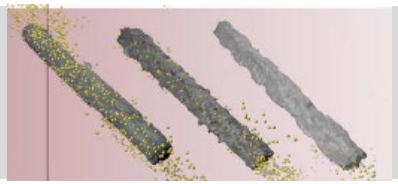
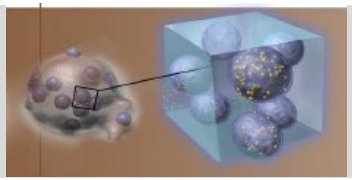
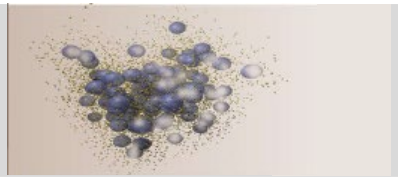
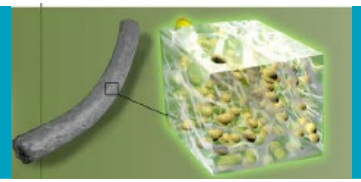
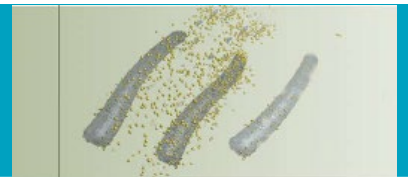
Sustained leakage control in repeat VEGF challenge animal model[2]

OCULAR THERAPEUTIX Retina experience redefined™

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

Comparison of Hydrogel vs Other Retinal Polymer Implants

	Implant (Full View)	Implant Dimensions (Length x Diameter)	Needle Size	Matrix Degradation & Release^^	Polymer Byproduct	Implant Remnants at 12 Months
OZURDEX abbvie		6mm x 0.46mm*	22-gauge*		Lactic acid and glycolic acid†	**Remnant** lasts ~12 months‡
EYP-1901 EyePoint Pharmaceuticals		**Two implants** with length of 8mm each¶	22-gauge#		>75 KDa polyvinyl alcohol‖	**Two remnants** last 18-24 months**
GB-102 graybug		N/A	27-gauge††		Lactic acid and glycolic acid††	N/A
OTX-TKI OCULAR THERAPEUTIX		**7mm x 0.40mm^**	**25-gauge^**		**Inert hydrogel PEG chains^**	**No remnants^^**

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

Schematic drawings, not drawn to scale or color, for illustrative purposes only; yellow or gray dots/spheres depict therapeutic agents released by implants

*. Li M, et al. *Heliyon.* 2022;8(12):e12219. †. Pellegrini GABP, et al. *Int J Retina Vitreous.* 2025;11(1):7. ‡. Kim JT, et al. *Retina*. 2020; 40(11):p 2226-2231. §. Schmit-Eilenberger VK. Clin *Ophthalmol.* 2015;9:801-811. ¶. Diameter of EYP-1901 unconfirmed; EyePoint Pharmaceuticals. Clinical Study Protocol. Protocol No. EYP-1901-201. Published January 25, 2024. ClinicalTrials.gov identifier: NCT05381948.. #. EyePoint Pharmaceuticals DAVIO2 Topline Results Conference Call, December 4, 2023. ‖. Wykoff CC, et al. *J Vitreoretin Dis*. 2024;8(5):577-586. **EyePoint Pharmaceuticals. TD Cowen 44th Annual Health Care Conference. March 5, 2024. https://investors.eyepointpharma.com/events-and-presentations. ††. Graybug Vision Inc. Clinical Study Protocol. Protocol No. GBV-102-002. Published September 8, 2020. ClinicalTrials.gov identifier: NCT03953079. ^. Blizzard CD, et al. Ocular Implant Containing a Tyrosine Kinase Inhibitor. US Patent 11,439,592 B2. September 13, 2022. ^^ Data on File 044. Ocular Therapeutix. 2026.
PEG, polyethylene glycol

OCULAR THERAPEUTIX Retina experience redefined™

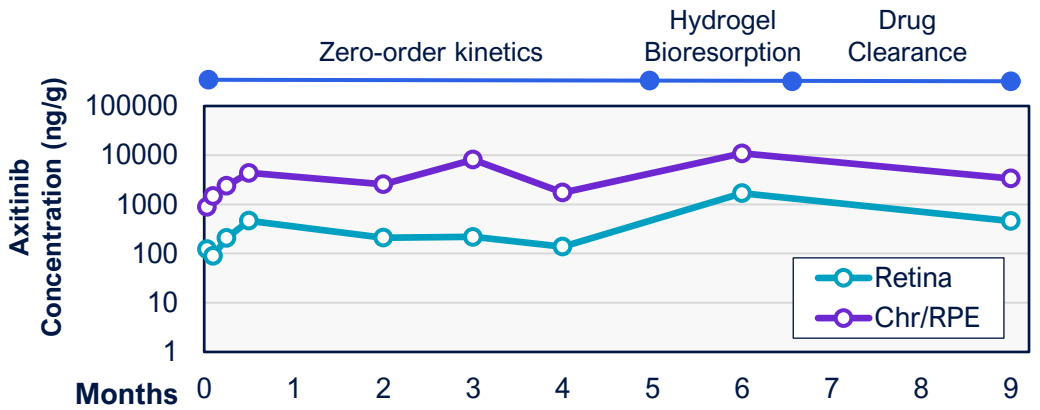
OTX-TKI is Designed to Release Axitinib and Maintain Intraocular Drug Levels Over Time

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.

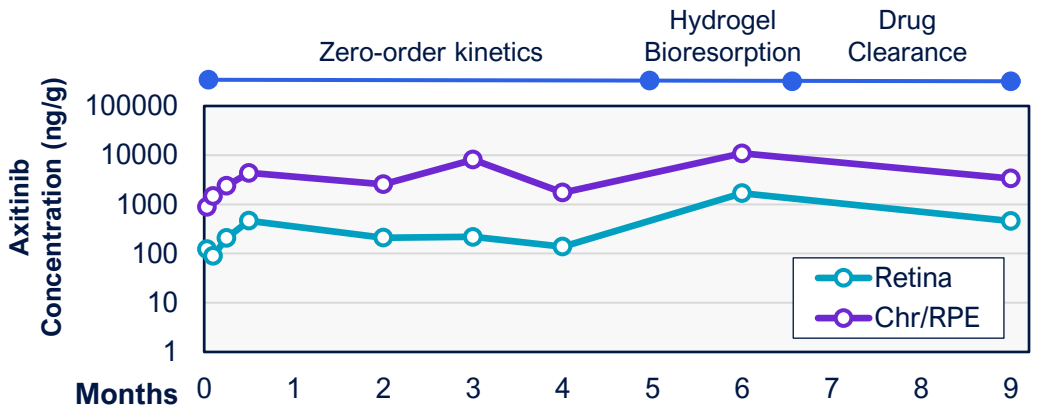
OTX-TKI is Designed to Release Axitinib and Maintain Intraocular Drug Levels Over Time with Complete Bioresorption

OTX-TKI In Vivo Delivery Profile[1]

Rapid, continuous and consistent axitinib delivery

Targeted drug delivery to retina and choroid

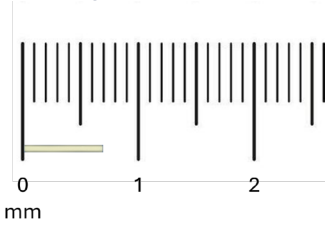
Axitinib concentrations following a single OTX-TKI in NHPs[1]

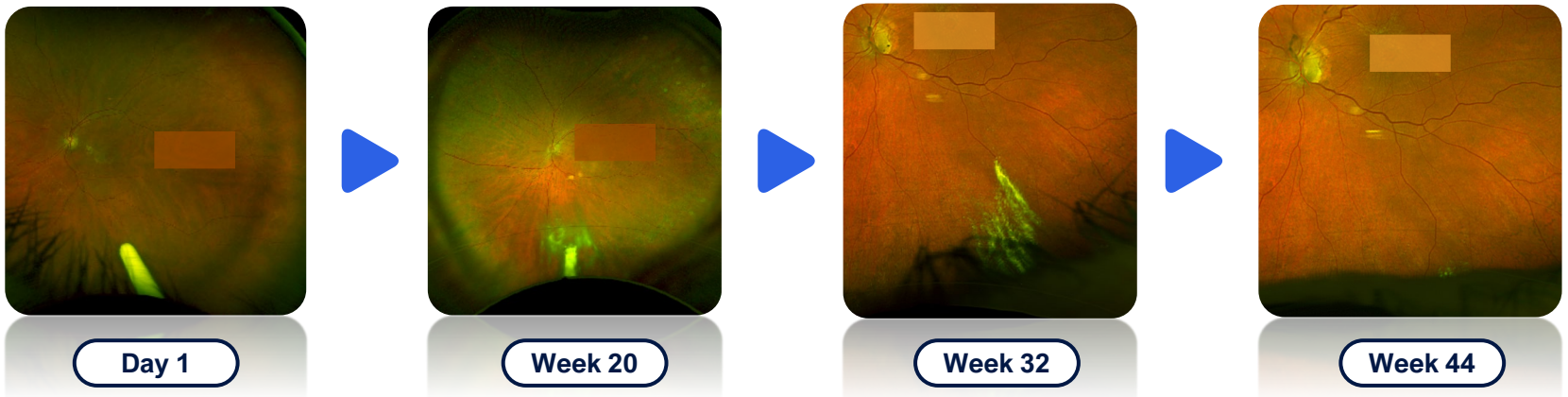


Hydrogel bioresorbs completely and predictably via hydrolysis for potential redosing[1-3]

Dry OTX-TKI Dimensions

7mm length, 0.4mm diameter





OCULAR THERAPEUTIX Retina experience redefined™

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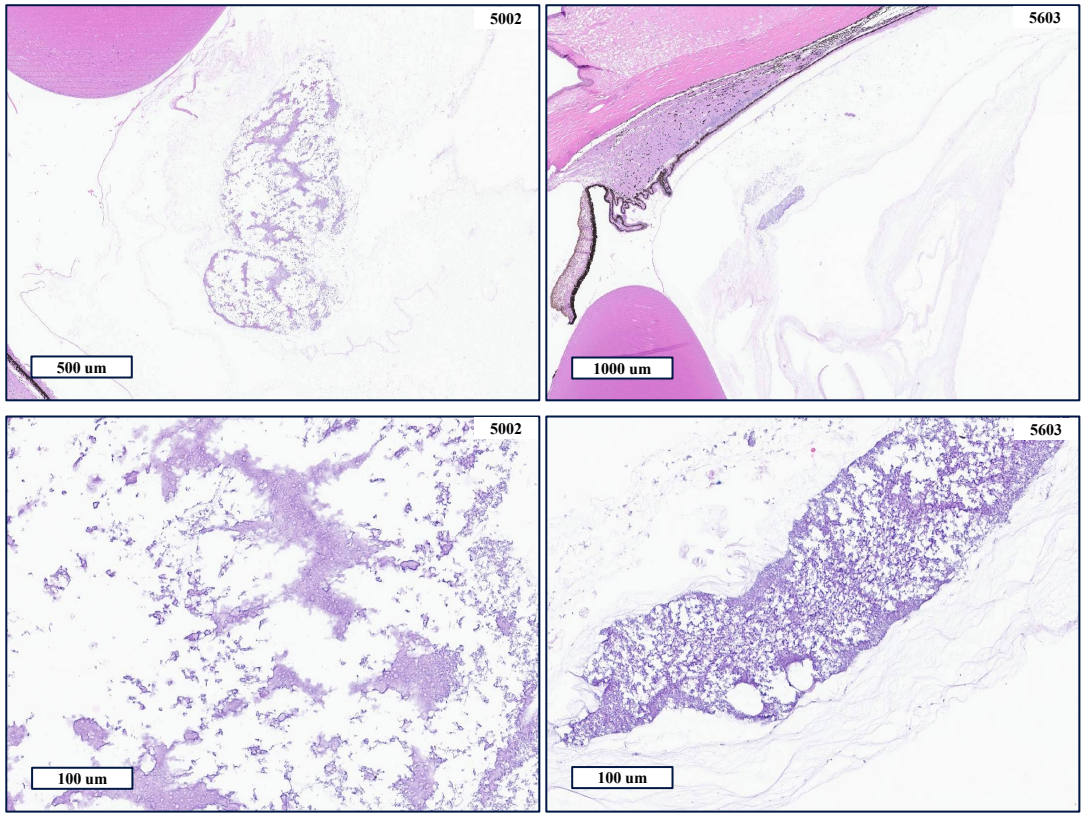
Chr, choroid; RPE, retinal pigment epithelium; NHP, non-human primate.

Histology of Ocular Tissues Demonstrates Axitinib Elution with No Inflammatory Cells

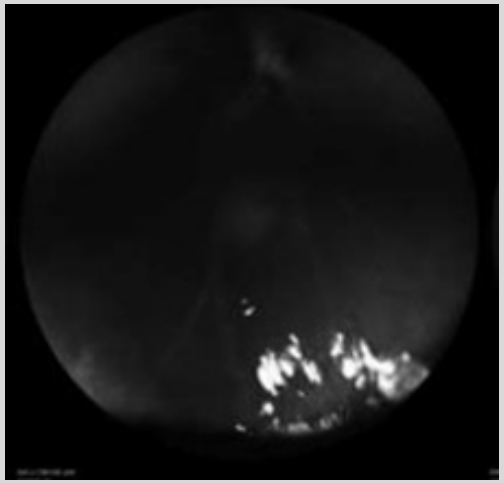
Histology of Ocular Tissues from 0.7 mg OTX-TKI in NHPs



Microscopic Findings

White, refractile, basophilic, granular axitinib in the vitreous

No inflammatory cells in vitreous, retina, or AC



From NHP Toxicity Study, not human picture

OCULAR THERAPEUTIX Retina experience redefined™

Data on File 043. Ocular Therapeutix; 2026
AC, anterior chamber; NHP, non-human primates

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.

SOL-1: Results

Dilsher S. Dhoot, MD

SOL: OTX-TKI Phase 3 Clinical Program in nAMD

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

Registrational Trials

SOL-1

Phase 3
Superiority Trial

Durability of a single OTX-TKI injection

SOL-R

Phase 3
Non-Inferiority Trial

Repeat dosing every 6 months

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

Extension Study

SOL-X

Open-Label Extension

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

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

OCULAR THERAPEUTIX Retina experience redefined

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

SOL: OTX-TKI Phase 3 Clinical Program in nAMD

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

Registrational Trials

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SOL-1

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SOL-R

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OCULAR THERAPEUTIX Retina experience redefined

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

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

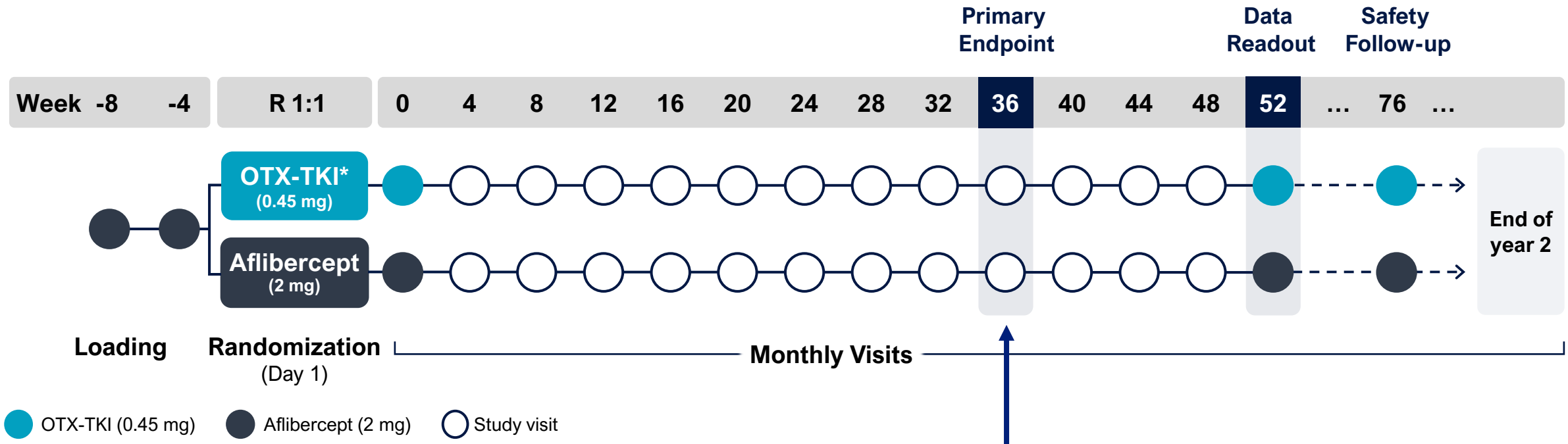
ClinicalTrials.gov. identifier: NCT06223958

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



Rescue Treatment 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

Primary Endpoint (Week 36)

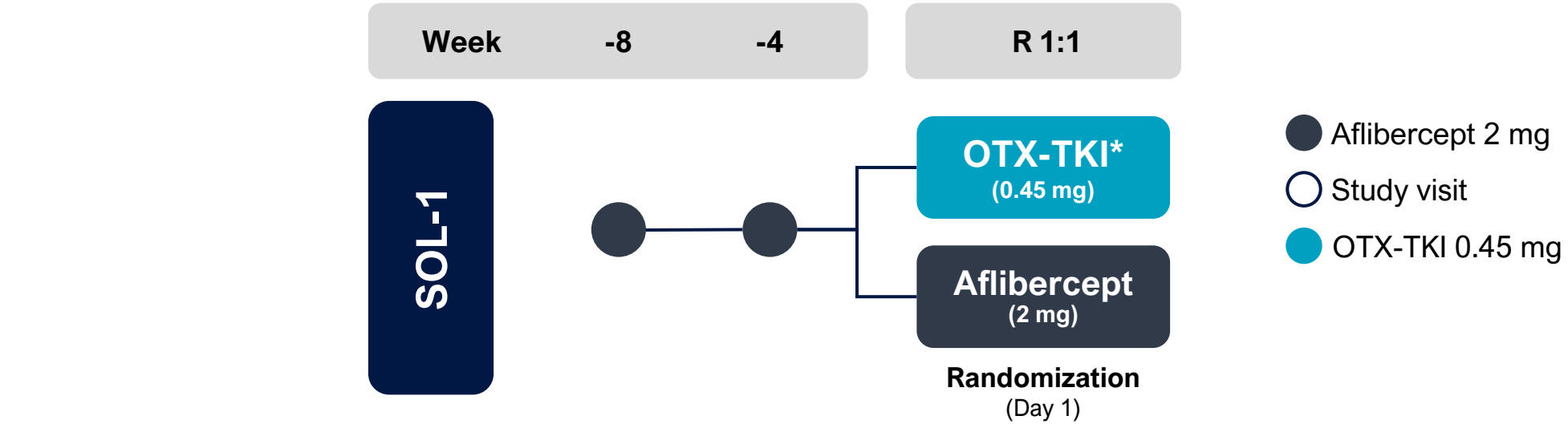
Proportion of subjects who maintained visual acuity, defined as <15 ETDRS letters of BCVA loss from baseline at Week 36

OCULAR THERAPEUTIX Retina experience redefined™

*No aflibercept injection is given at baseline
ClinicalTrials.gov. identifier: NCT06223958
BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study

Eligibility and Enrollment Criteria

Key Inclusion Criteria



Enrollment Criteria
Screening Visit (Week -8)

Treatment naïve CNV due to nAMD

BCVA ≥54 ETDRS letters
(~20/80 Snellen equivalent)

CSFT of ≤500 µm

Randomization Criteria
Baseline Visit (Day 1)

BCVA gain ≥10 ETDRS letters

- OR -

BCVA ≥84 ETDRS letters
(~20/20 Snellen equivalent)

CSFT of ≤350 µm

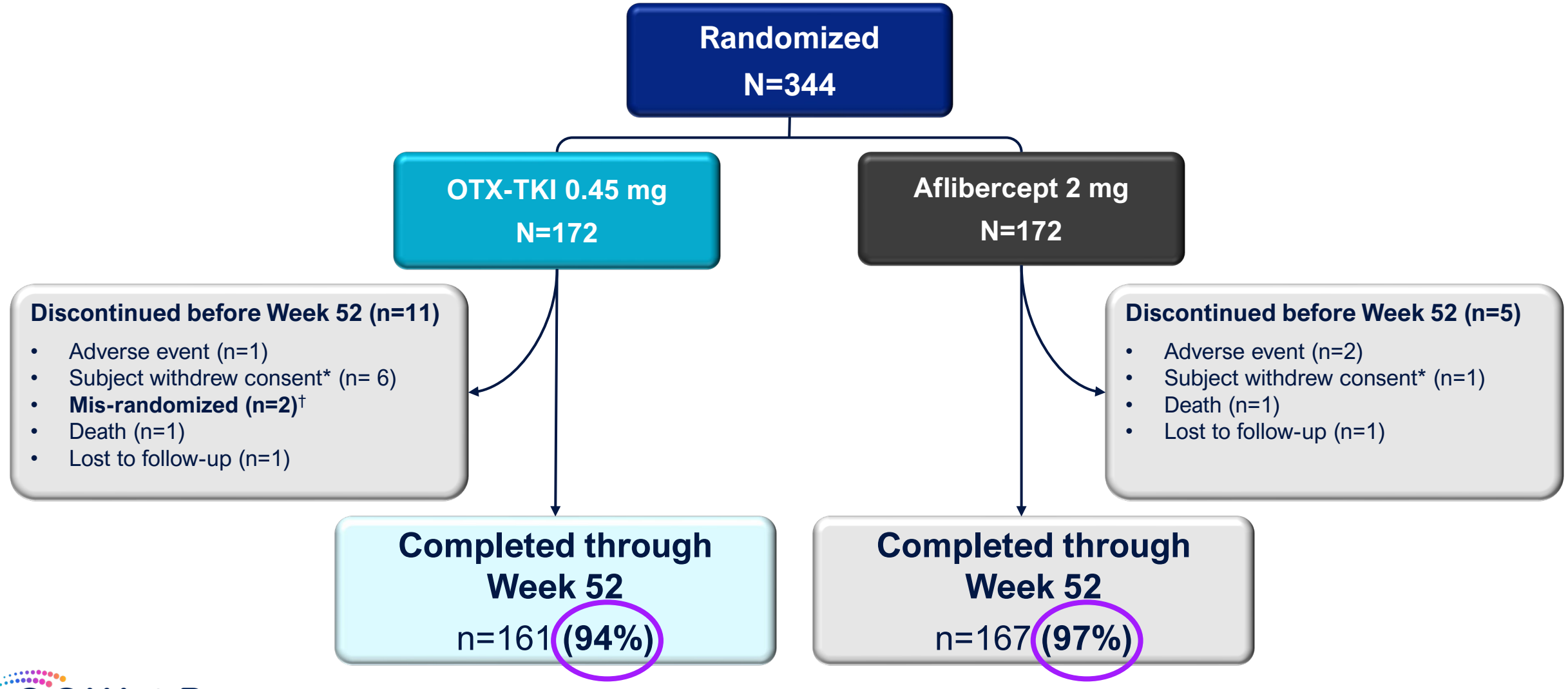
*No aflibercept injection is given at baseline

ClinicalTrials.gov. identifier: NCT06223958

CNV, choroidal neovascularization; nAMD, neovascular age-related macular degeneration; BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium

Strong Subject Retention Maintained through Week 52

Subject Disposition



* Reasons included: personal reason, no reason, travel, offered another treatment at a different practice; only Day 1 completed, subject refused week 52 assessment
† Subjects did not receive study treatment and were not included in the full analysis set

Excellent Vision at Baseline; Majority Demonstrated ≥10-letter Gain from Screening

SOL-1

Best-Corrected Visual Acuity

Screening Visit *(Week -8)*

Study Eye Characteristics	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

Baseline *(Randomization)*

Study Eye Characteristics	OTX-TKI 0.45 mg N = 172	Aflibercept 2 mg N = 172
BCVA, ETDRS letter score, mean (SD) Snellen Equivalent	80.8 (7.6) ~20/25	79.2 (7.9) ~20/25
Change from Screening to Baseline, n (%) ≥ 10 ETDRS letter gain ≥84 ETDRS letters (~20/20)	 107 (62.9) 63 (37.1)	 114 (67.1) 56 (32.9)

OCULAR THERAPEUTIX Retina experience redefined™

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; SD, standard deviation.

Anatomic Improvement Observed After Two Aflibercept Injections

SOL-1

Central Subfield Thickness

Screening Visit *(Week -8)*

Study Eye Characteristics	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
CSFT, µm, mean (SD)	303.6 (72.5)	302.7 (78.3)

Baseline *(Randomization)*

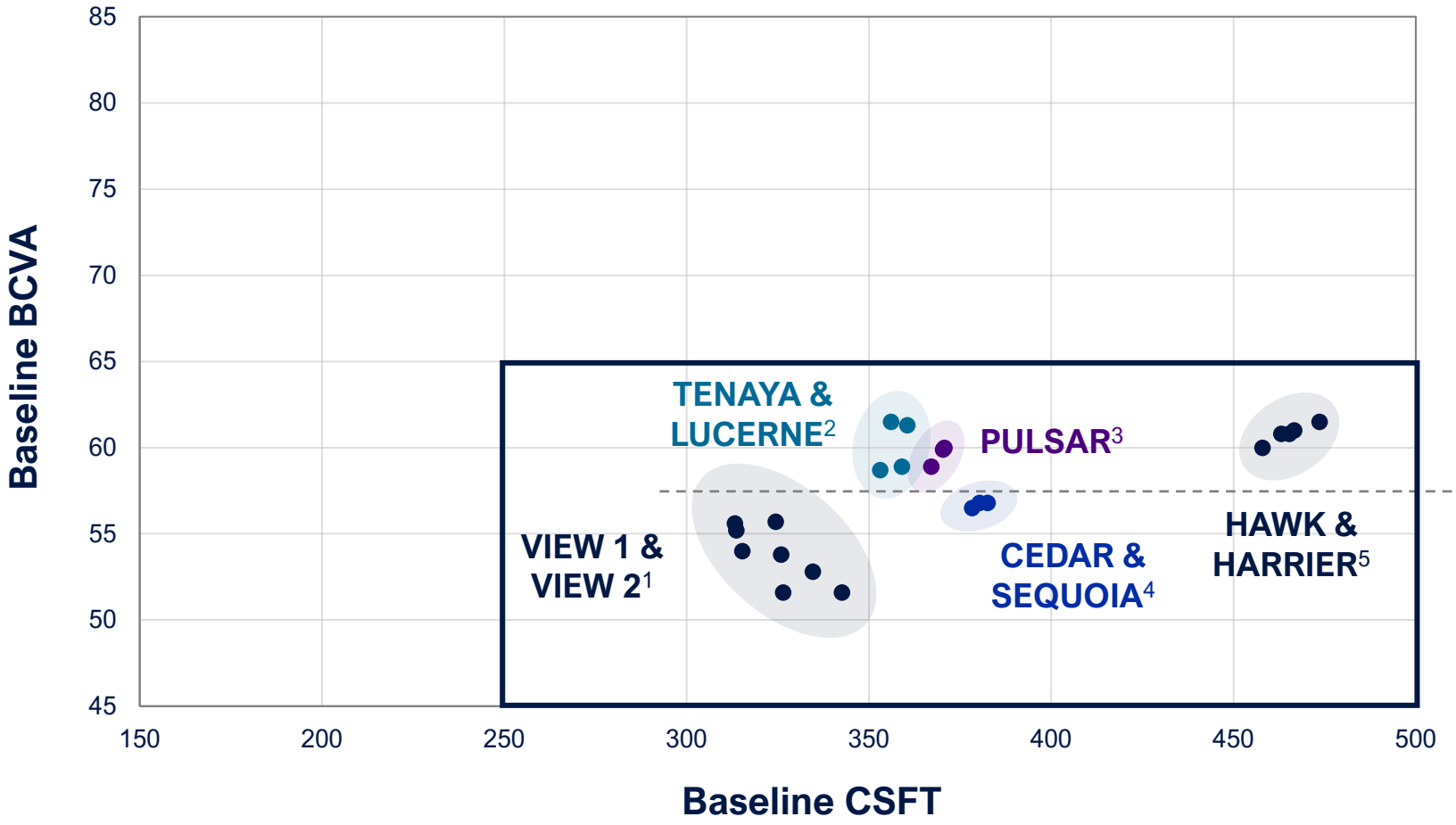
Study Eye Characteristics	OTX-TKI 0.45 mg N = 172	Aflibercept 2 mg N = 172
BCVA, ETDRS letter score, mean (SD) Snellen Equivalent	80.8 (7.6) ~20/25	79.2 (7.9) ~20/25
CSFT, µm, mean (SD)	219.3 (37.1)	226.8 (42.1)

OCULAR THERAPEUTIX Retina experience redefined

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; CSFT, central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; SD, standard deviation

SOL-1 Evaluates a Distinct nAMD Cohort with Excellent Baseline Vision

Baseline BCVA Across nAMD Trials



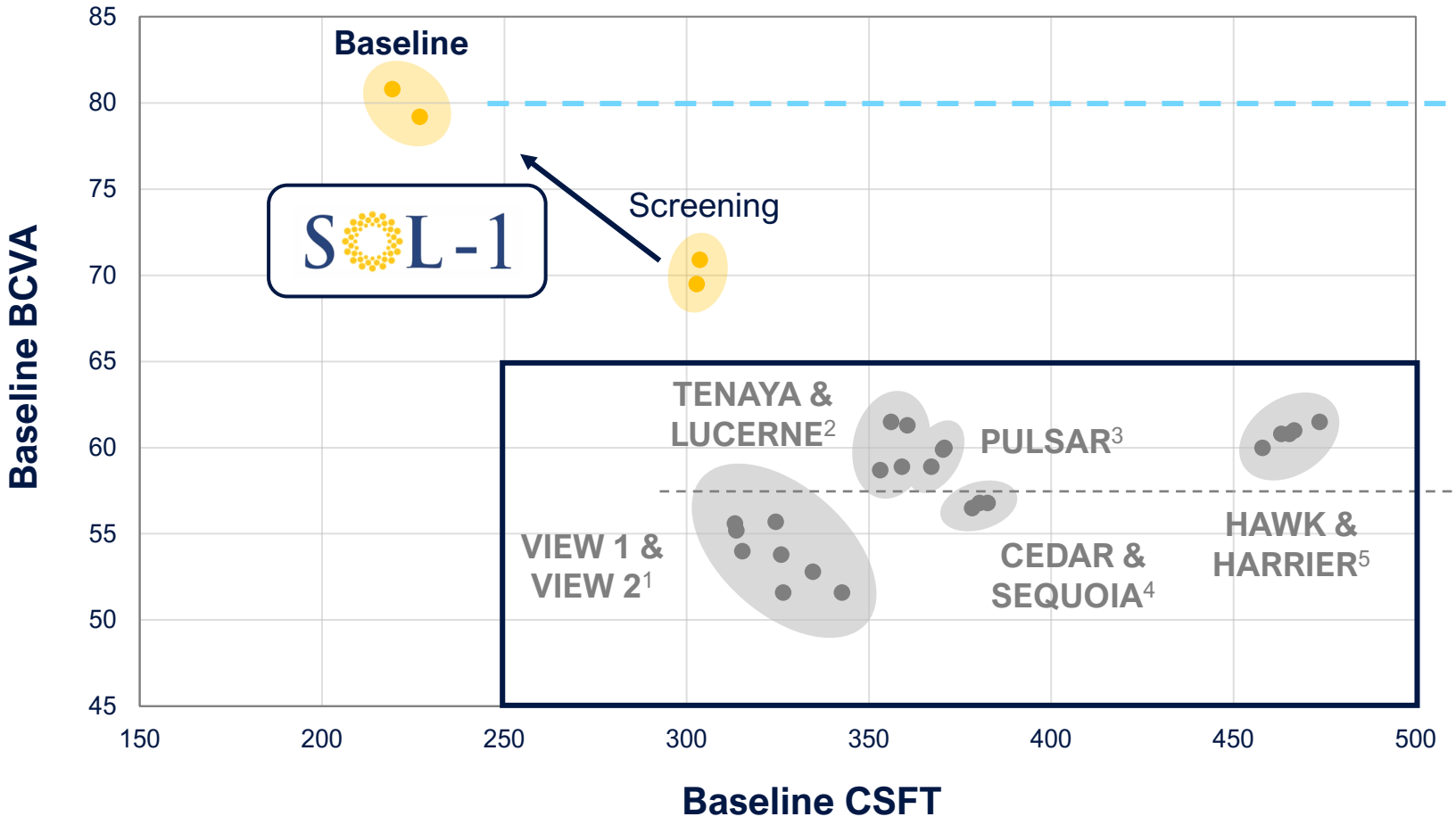
nAMD Trials
mean BCVA: **52 to 62 letters (~20/100 to 20/60)**

OCULAR THERAPEUTIX Retina experience redefined

1. Heier JS, et al. *Ophthalmology*. 2012;119(12):2537-2548. 2. Heier JS, et al. *Lancet*. 2022;399(10326):729-740. 3. Lanzetta P, et al. *Lancet*. 2024;403(10432):1141-1152. 4. Kunimoto D, et al. *Ophthalmology*. 2020;127(10):1331-1344. 5. Dugel PU, et al. *Ophthalmology*. 2020;127(1):72-84.
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; nAMD, neovascular age-related macular degeneration

SOL-1 Evaluates a Distinct nAMD Cohort with Excellent Baseline Vision

Baseline BCVA Across nAMD Trials



SOL-1
mean BCVA: **81 letters (~20/25)**
mean CSFT: **219 µM**

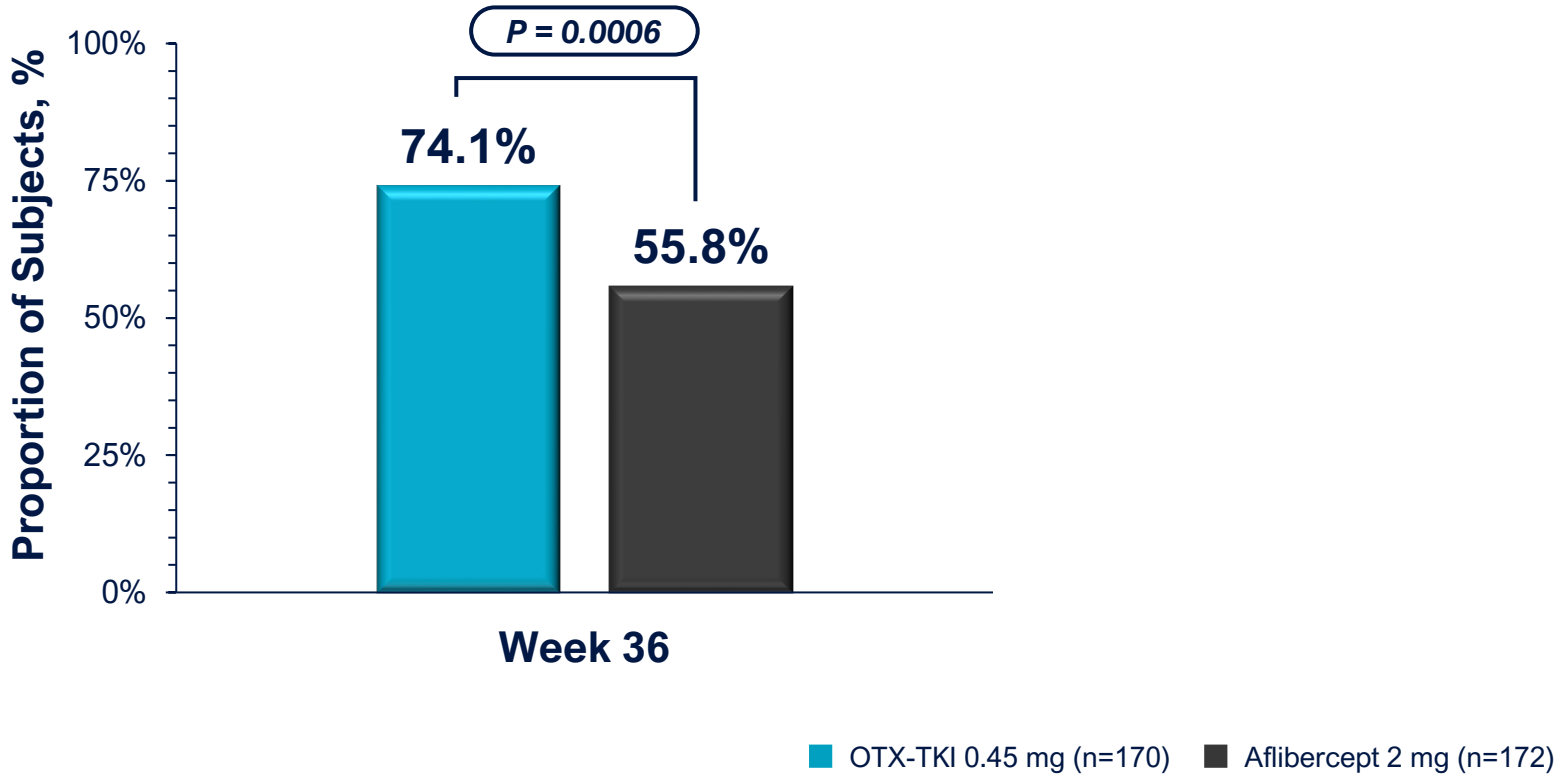
nAMD Trials
mean BCVA: **52 to 62 letters (~20/100 to 20/60)**

OCULAR THERAPEUTIX Retina experience redefined

1. Heier JS, et al. *Ophthalmology*. 2012;119(12):2537-2548. 2. Heier JS, et al. *Lancet*. 2022;399(10326):729-740. 3. Lanzetta P, et al. *Lancet*. 2024;403(10432):1141-1152. 4. Kunimoto D, et al. *Ophthalmology*. 2020;127(10):1331-1344. 5. Dugel PU, et al. *Ophthalmology*. 2020;127(1):72-84.
BCVA, best-corrected visual acuity; CSFT, central subfield thickness; nAMD, neovascular age-related macular degeneration

Primary Endpoint Successfully Met

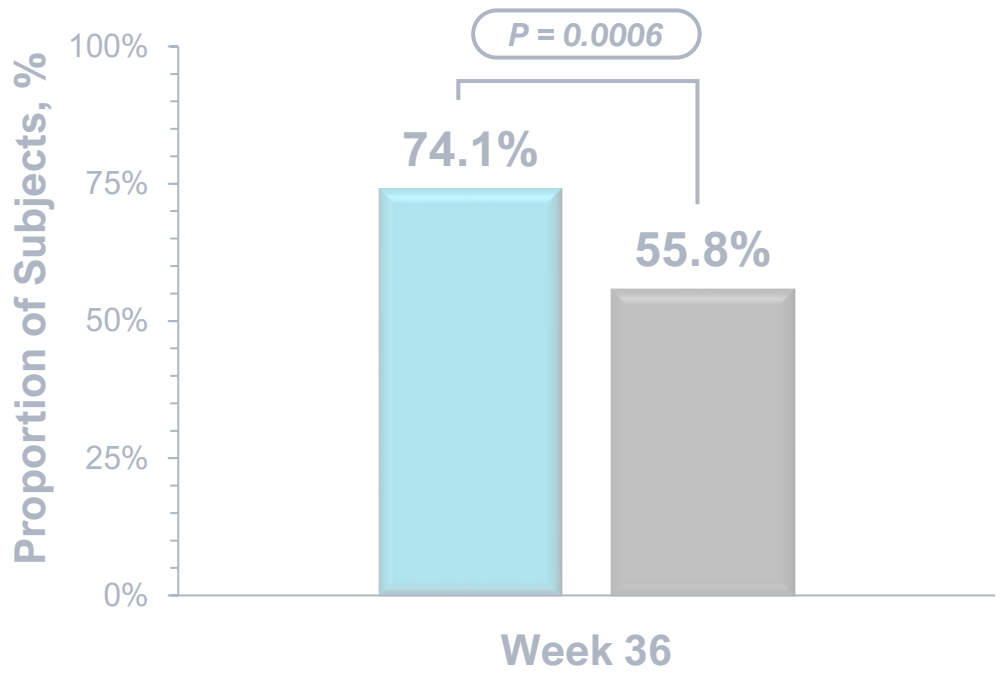
Statistically Significant Higher Proportion of Subjects Maintained Visual Acuity* with OTX-TKI vs. Aflibercept 2 mg at Week 36

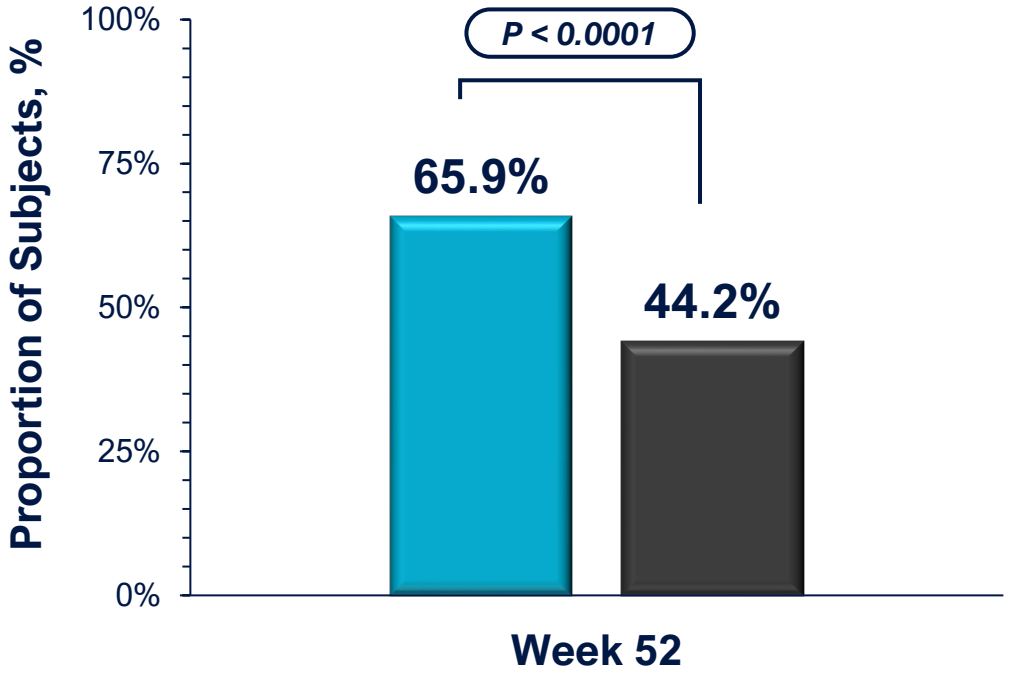


*Maintenance of vision defined as proportion of subjects who maintain visual acuity, a loss of <15 ETDRS letters of BCVA from baseline

Difference in Proportion of Subjects Maintaining Visual Acuity Sustained Through Week 52

Key Secondary Endpoint: Maintenance of Visual Acuity* at Week 52



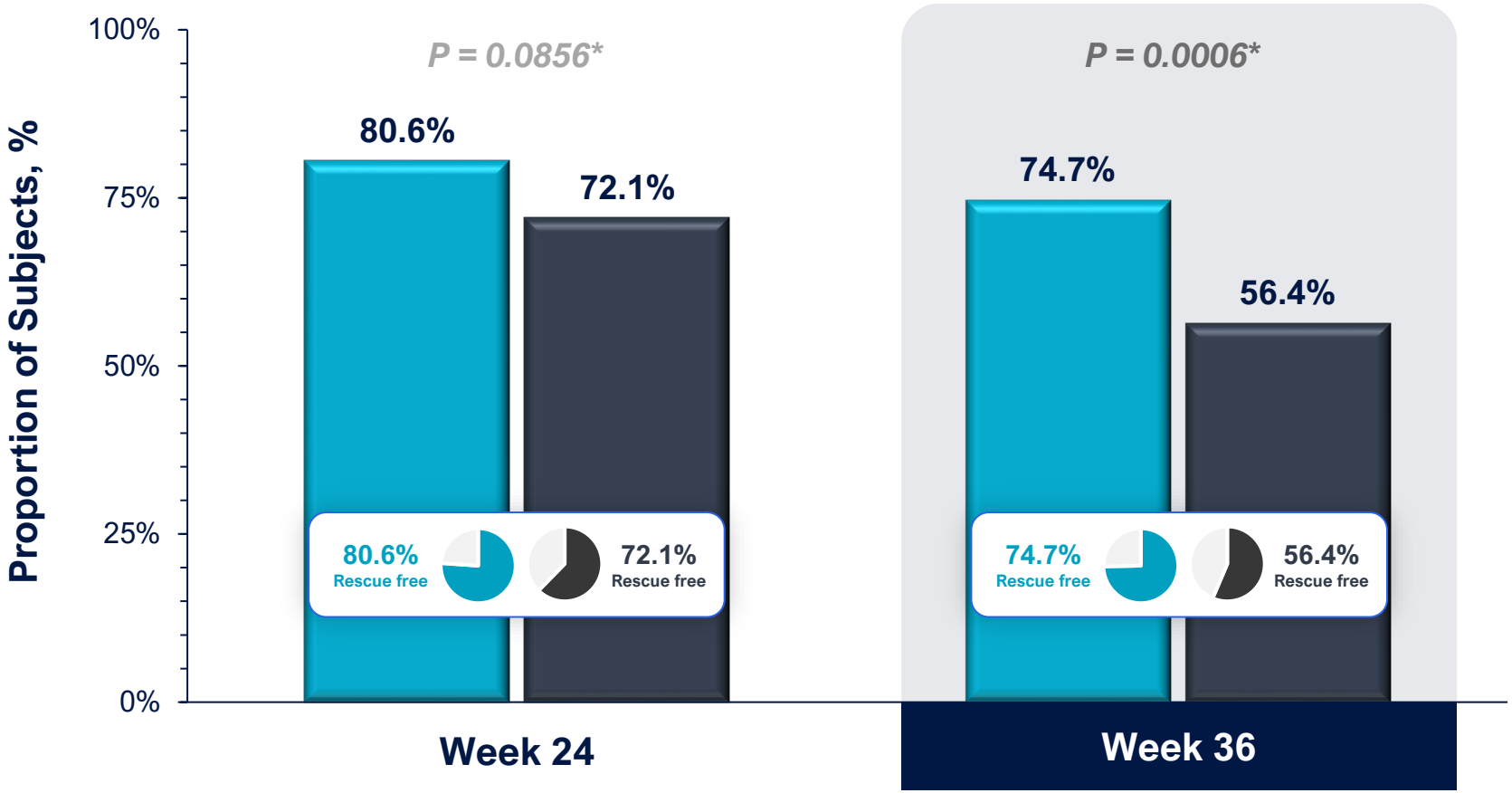


OTX-TKI 0.45 mg (n=170) Aflibercept 2 mg (n=172)

*Maintenance of vision defined as proportion of subjects who maintain visual acuity, a loss of <15 ETDRS letters of BCVA from baseline

Most Subjects (~75%) in the OTX-TKI Arm Did Not Receive Rescue Injections

Post Hoc Analysis: Proportion of Rescue-Free Subjects

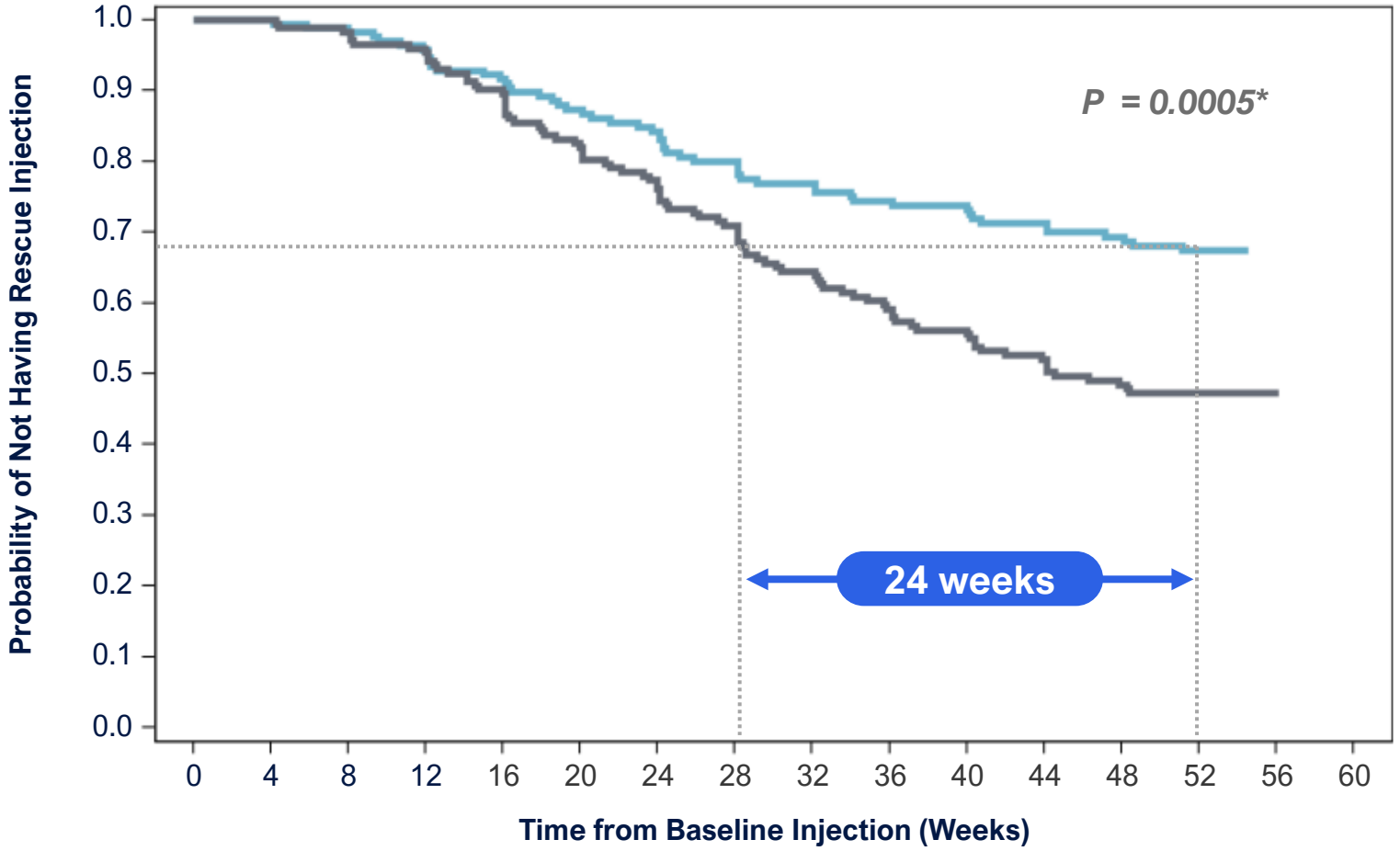


Rescue-free subjects include those who did not require rescue injections as specified by the protocol
Full analysis set; *Descriptive p-values

OTX-TKI Extended Durability, Significantly Delaying First Rescue Injection

SOL-1

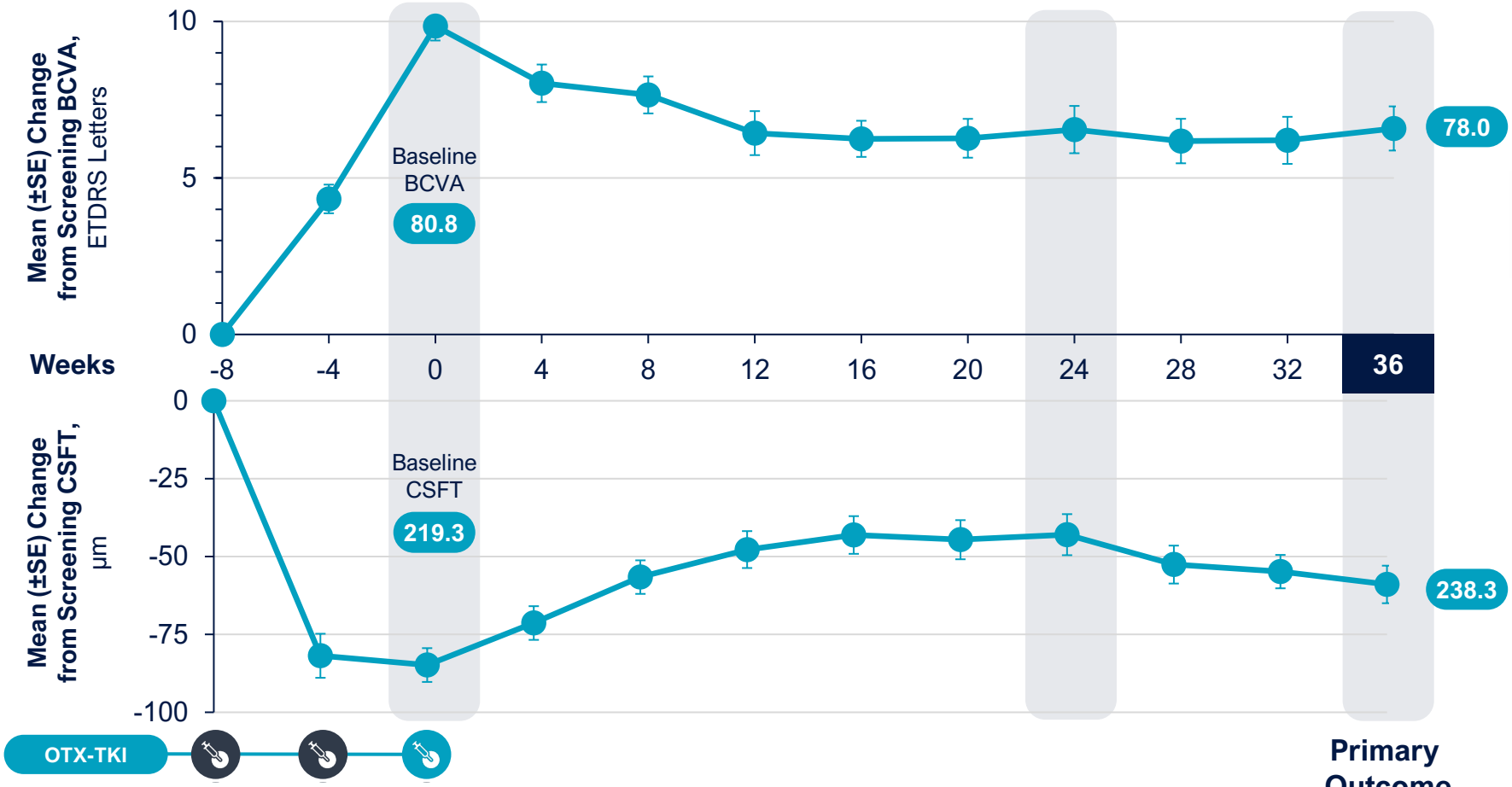
Secondary Endpoint: Time to First Rescue Treatment



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

On Average, OTX-TKI Subjects Maintained Vision and Anatomy, with Most Remaining Rescue-Free

Post Hoc Analysis: Mean Change in BCVA and CSFT from Screening



74.7%
Rescue free

Full analysis set. For subjects who received any rescue injections, their observed BCVA and CSFT values after the 1st rescue injection are set to missing

Baseline measurements are the last non-missing measurement prior to the study drug injection on Day 1

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; SE, standard error

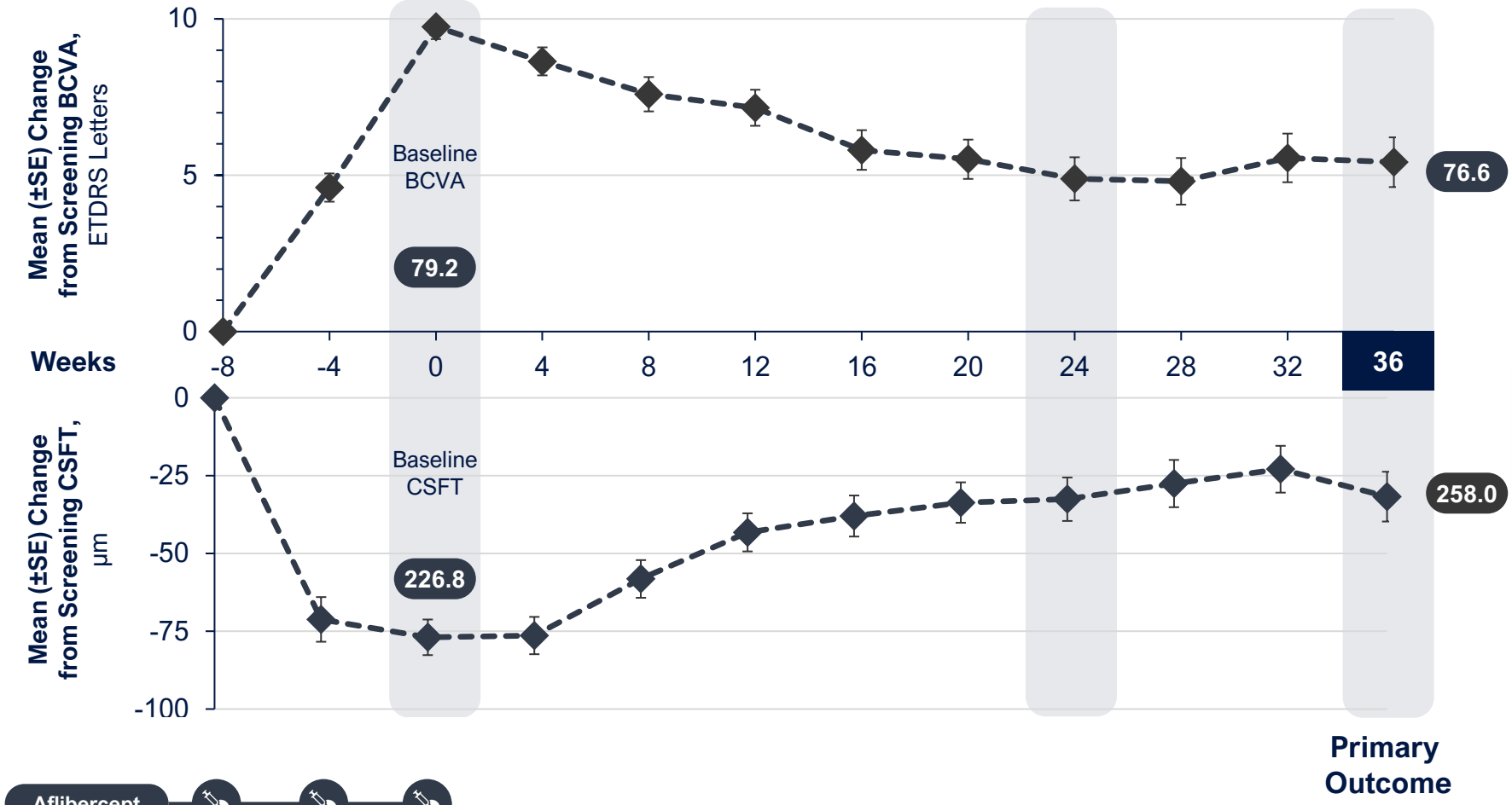
OTX-TKI 0.45 mg (n=170)

Aflibercept 2 mg (n=172)

On Average, OTX-TKI Subjects Maintained Vision and Anatomy, with Most Remaining Rescue-Free

SOL-1

Post Hoc Analysis: Mean Change in BCVA and CSFT from Screening



Aflibercept

Full analysis set. For subjects who received any rescue injections, their observed BCVA and CSFT values after the 1st rescue injection are set to missing

Baseline measurements are the last non-missing measurement prior to the study drug injection on Day 1

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; SE, standard error

OCULAR THERAPEUTIX Retina experience redefined

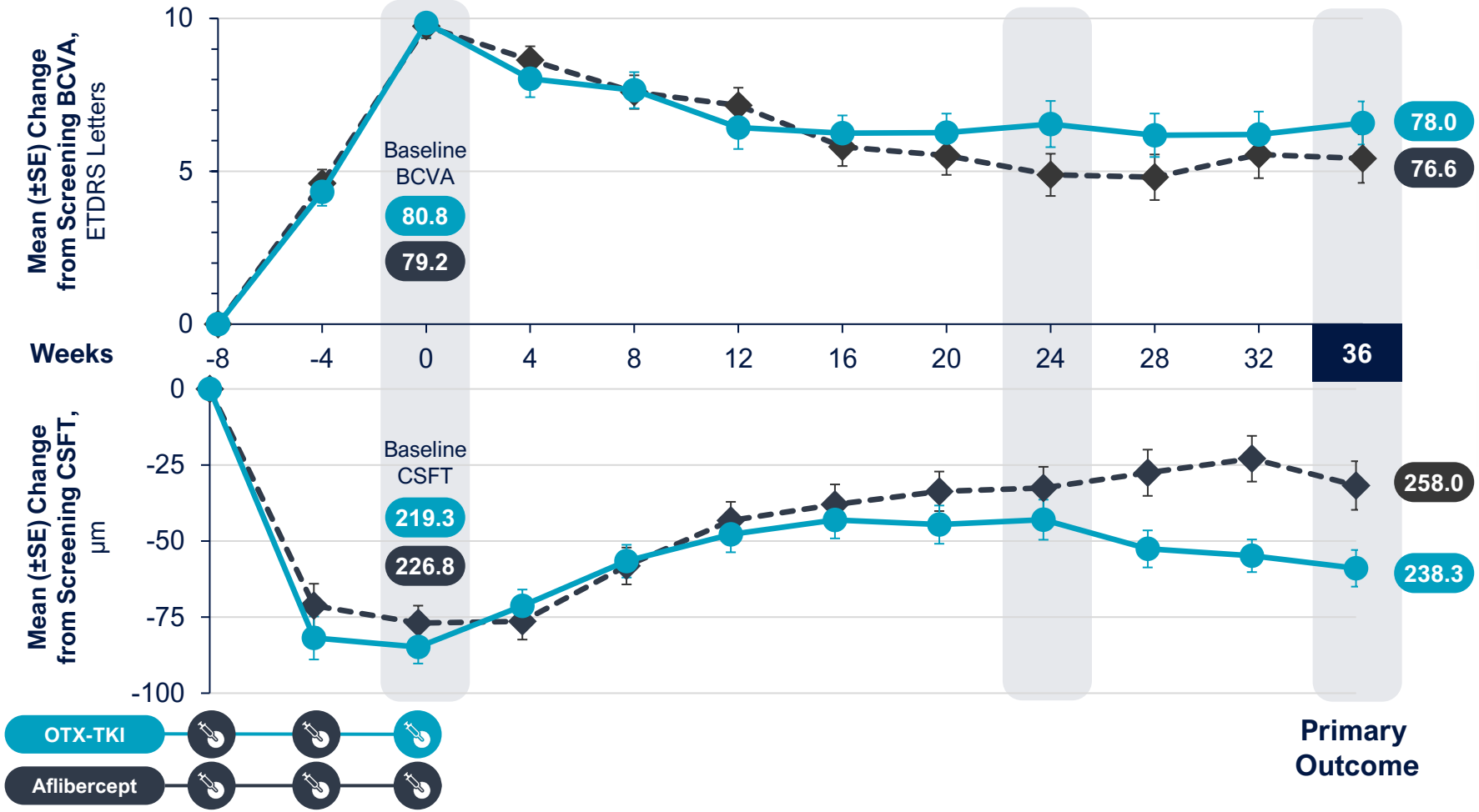
OTX-TKI 0.45 mg (n=170)

Aflibercept 2 mg (n=172)

On Average, OTX-TKI Subjects Maintained Vision and Anatomy, with Most Remaining Rescue-Free

SOL-1

Post Hoc Analysis: Mean Change in BCVA and CSFT from Screening



74.7%
Rescue free

56.4%
Rescue free

OCULAR THERAPEUTIX Retina experience redefined

Full analysis set. For subjects who received any rescue injections, their observed BCVA and CSFT values after the 1st rescue injection are set to missing

Baseline measurements are the last non-missing measurement prior to the study drug injection on Day 1

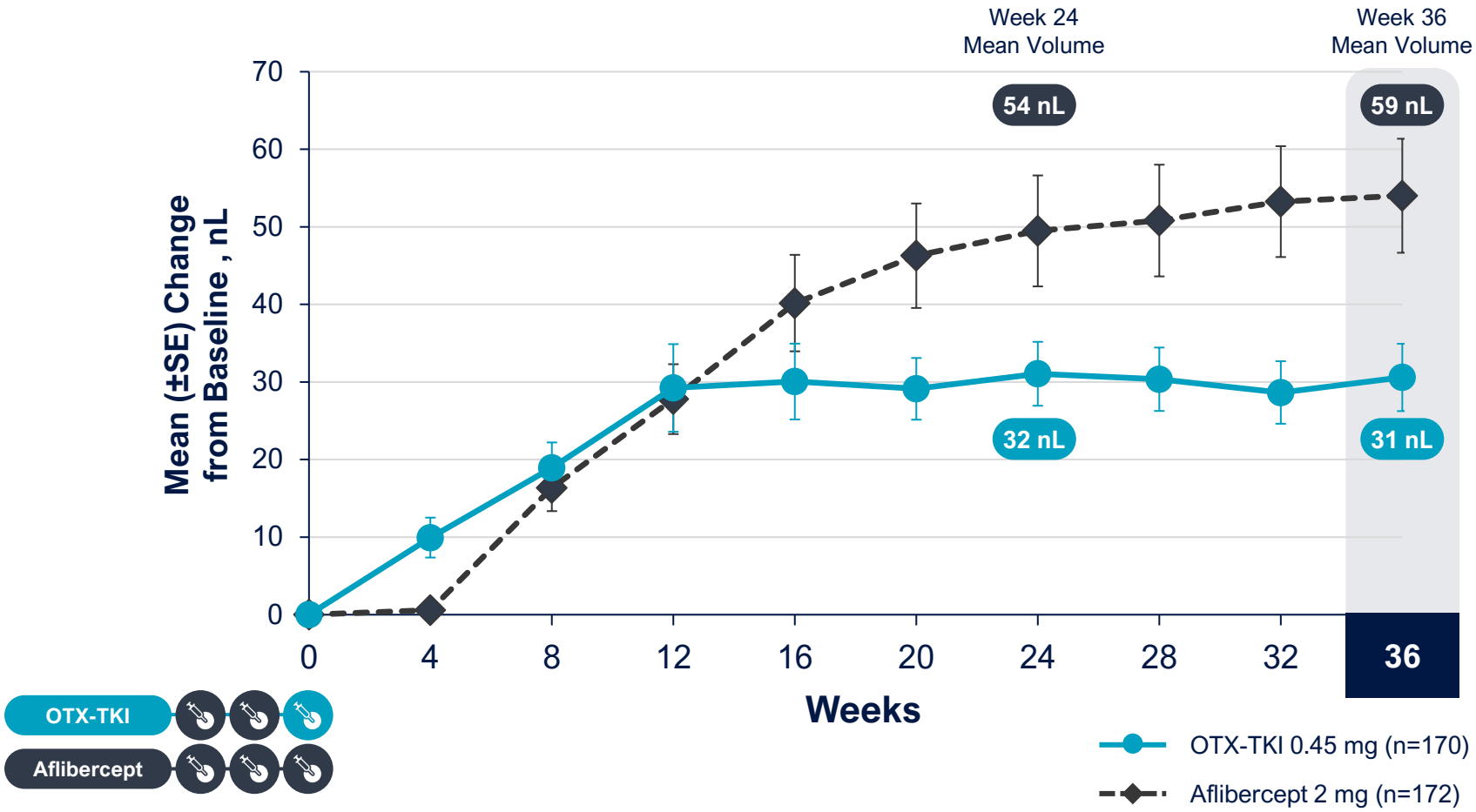
BCVA, best-corrected visual acuity; CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium; ETDRS, Early Treatment Diabetic Retinopathy Study; SE, standard error

OTX-TKI 0.45 mg (n=170)

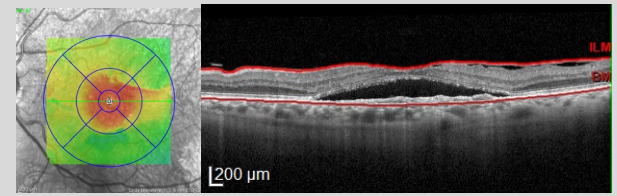
Aflibercept 2 mg (n=172)

OTX-TKI Delivered Sustained Fluid Control

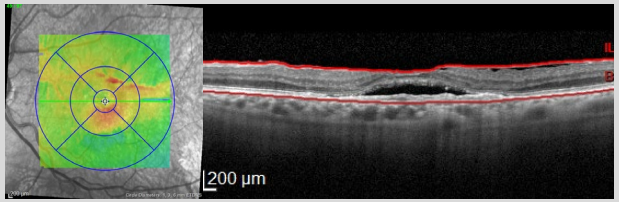
Prespecified Exploratory Analysis: Mean Change in Intra-Retinal and Sub-Retinal Fluid Volume



Total Fluid Volume: 60 nL



Total Fluid Volume: 30 nL



OCULAR THERAPEUTIX Retina experience redefined

Full analysis set
SE, standard error

No Treatment or Procedure Related SAEs

Non-Ocular and Ocular Adverse Events in the Study Eye

Subjects with AEs Through Week 52, n (%)	OTX-TKI 0.45 mg n = 170	Aflibercept 2 mg n = 172
Non-ocular AEs		
≥ 1 AE	84 (49.4)	73 (42.4)
≥ 1 SAE	19 (11.2)	21 (12.2)
≥ 1 treatment-related AE	0	0
≥ 1 treatment-related SAE	0	0
≥ 1 study procedure-related AE	1 (0.6)	0
≥ 1 study procedure-related SAE	0	0
AE leading to study discontinuation	3 (1.8)	3 (1.7)
AE leading to death*	2 (1.2)	1 (0.6)
Ocular AEs in the study eye		
≥ 1 AE	90 (52.9)	58 (33.7)
≥ 1 SAE†	1 (0.6)	0
≥ 1 treatment-related AE	15 (8.8)	1 (0.6)
≥ 1 treatment-related SAE	0	0
≥ 1 study procedure-related AE	15 (8.8)	7 (4.1)
≥ 1 study procedure-related SAE	0	0
Ocular AE leading to study discontinuation	0	0

*Stroke (day 103); worsening of metastatic melanoma (day 319); lung cancer metastatic (day 503)

†Severe vision loss due to 3+ PSC cataract, 78 ETDRS letters at baseline, recovered to 70 ETDRS letters after cataract surgery

AE, adverse event; SAE, serious AE; PSC, posterior subcapsular cataract; ETDRS, Early Treatment Diabetic Retinopathy Study

OTX-TKI was Generally Well Tolerated

Ocular Adverse Events in the Study Eye

Subjects with Ocular AEs (> 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)

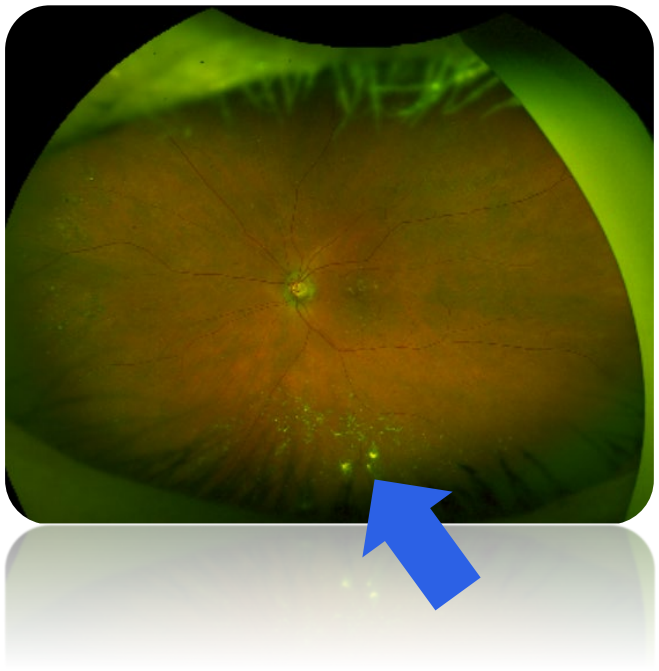
- Nine IOI events observed in study eyes of 7 subjects in the OTX-TKI arm
  - All cases were mild or moderate in severity and resolved
- **There were no cases of endophthalmitis, occlusive or non-occlusive retinal vasculitis**

AE, adverse event; IOI, intraocular inflammation

Appearance of Floaters May Correspond to Hydrogel Dissolution and Drug Elution

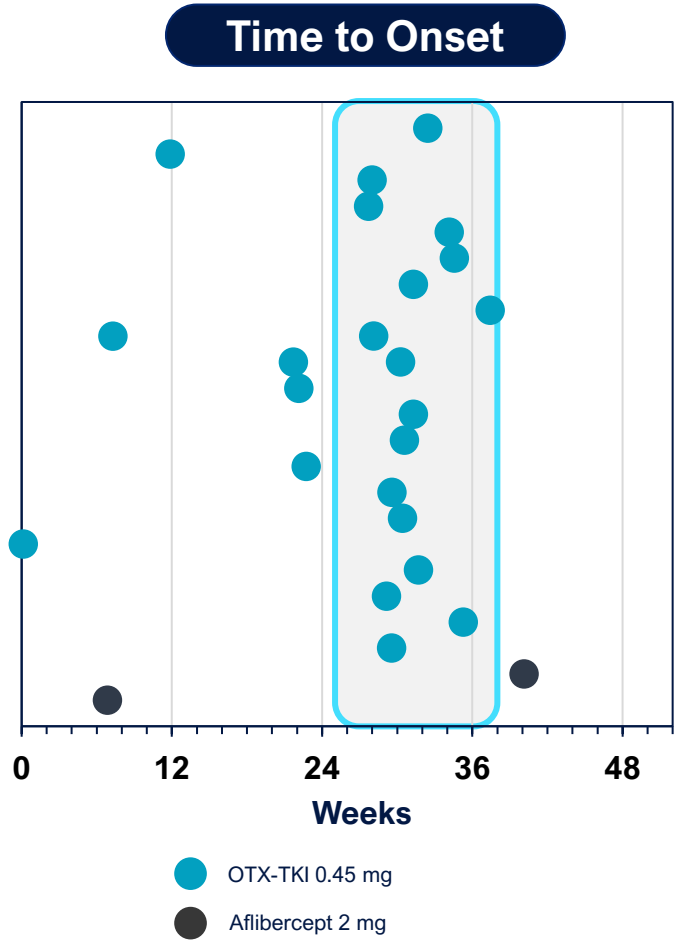
SOL-1

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

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

SOL-1

Superiority Primary Endpoint Successfully Met

First trial to demonstrate durability ≥ 9 months

~75% of subjects treated with OTX-TKI did not receive rescue treatments by Week 36

Unmatched Durability

Visual and anatomic stability with OTX-TKI

On average, OTX-TKI subjects maintained visual and anatomical outcomes, with most remaining rescue-free

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

OCULAR THERAPEUTIX Retina experience redefined

Rescue-free subjects include those who did not require rescue injections as specified by the protocol

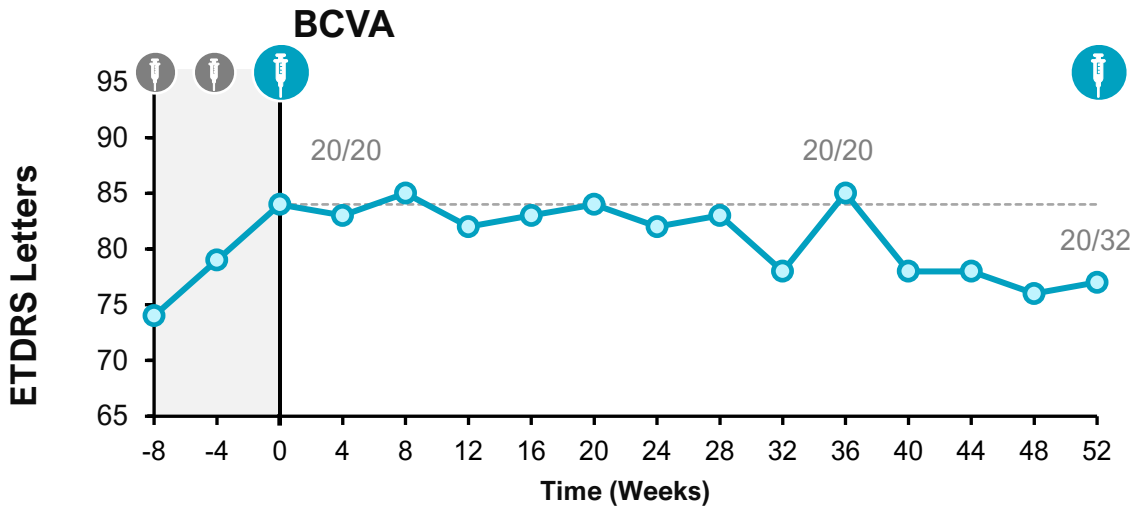
SOL-1

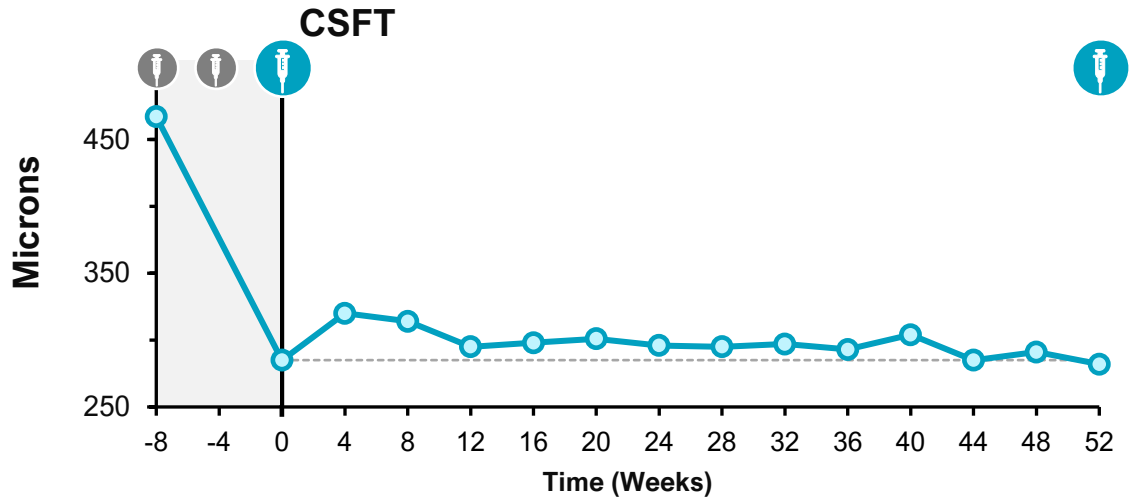
Clinical Evidence

Lejla Vajzovic, MD

OCULAR THERAPEUTIX Retina experience redefined

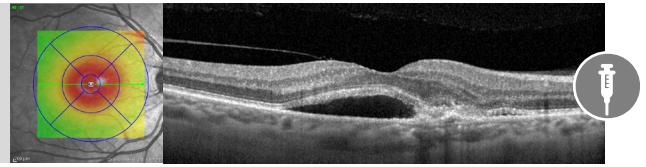
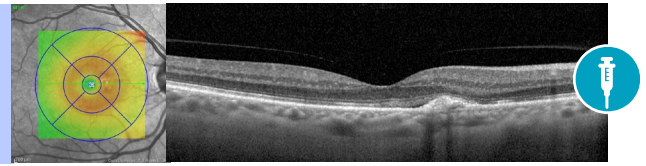
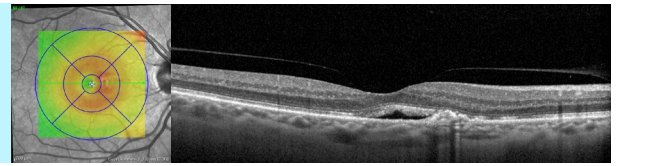
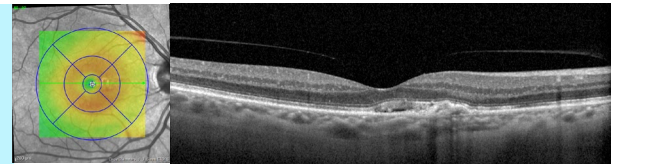
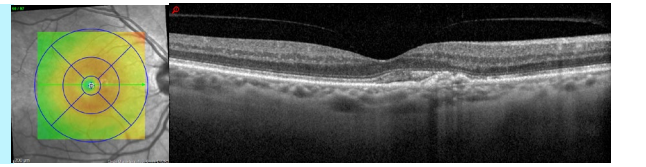
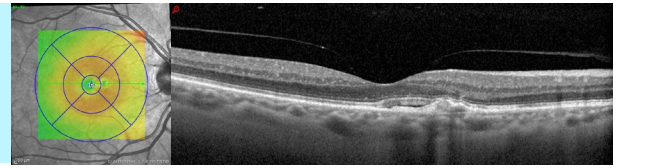
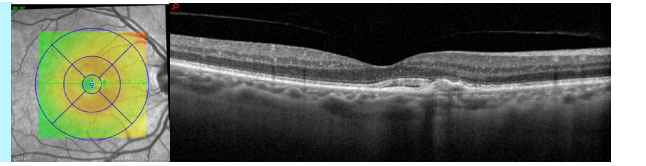
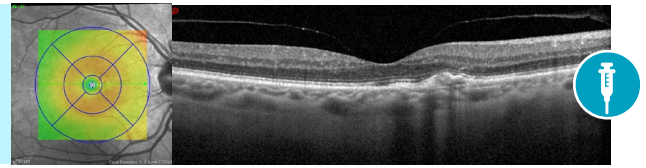
OTX-TKI Case 1





Screening Aflibercept (2mg)

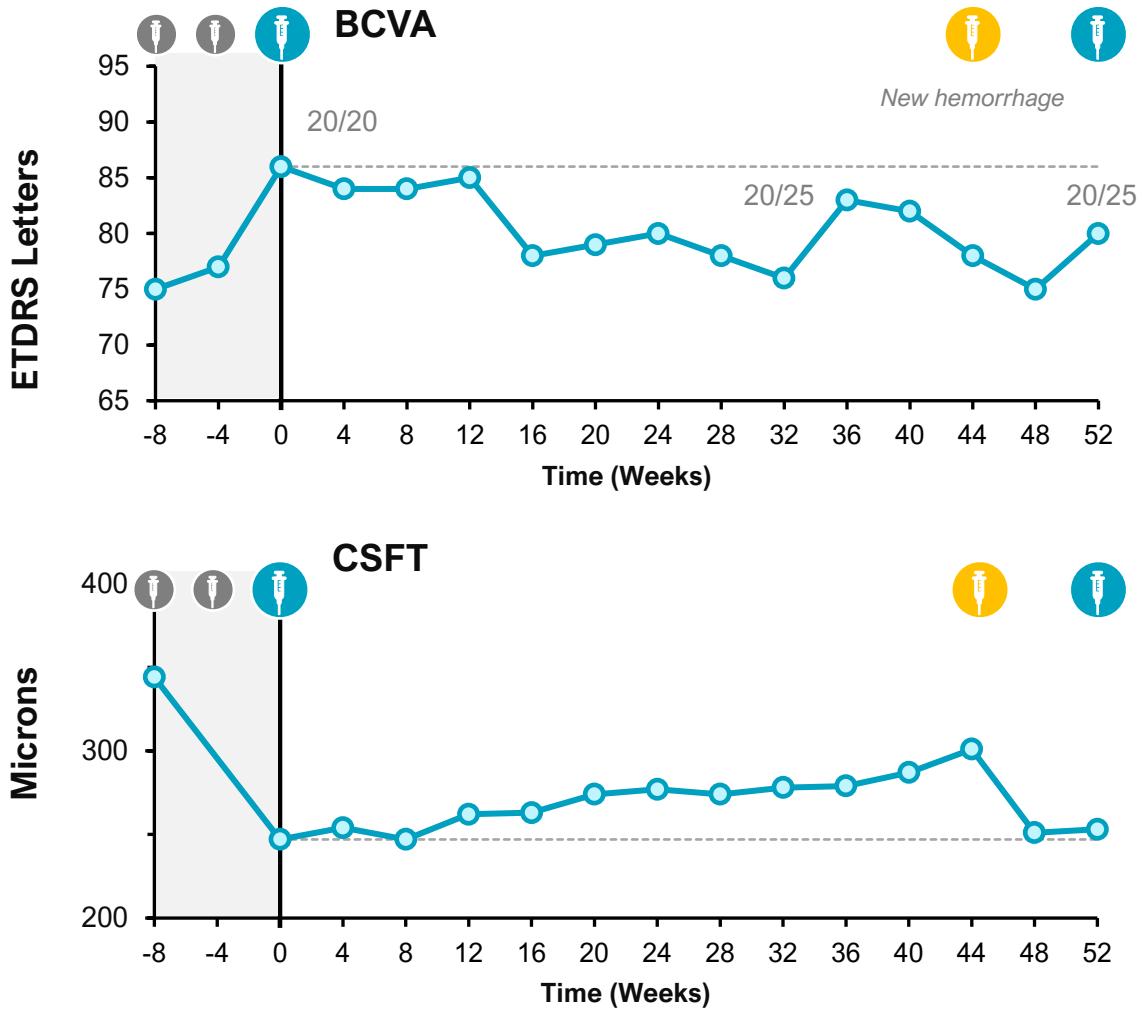
OTX-TKI (0.45mg)

-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

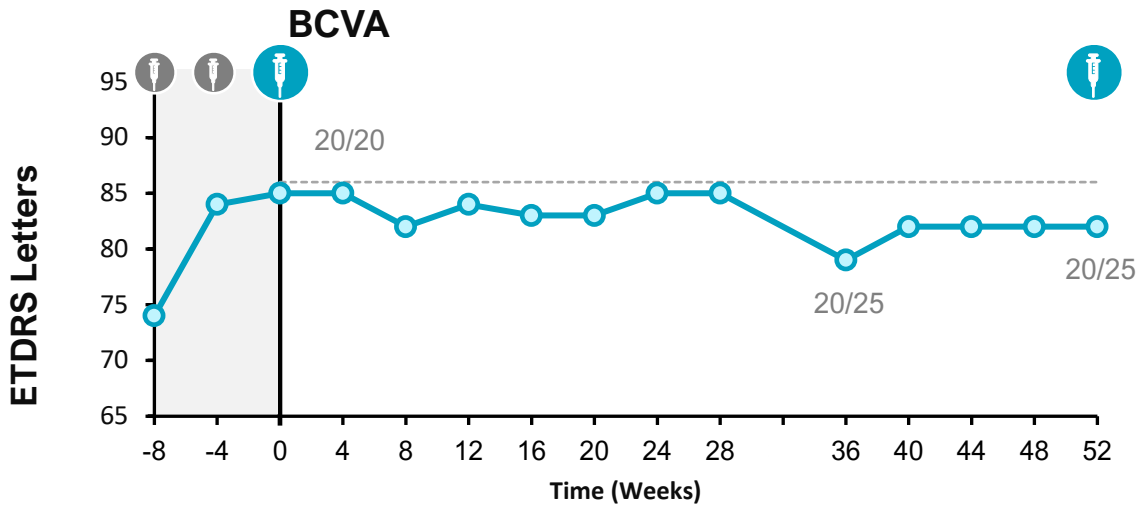


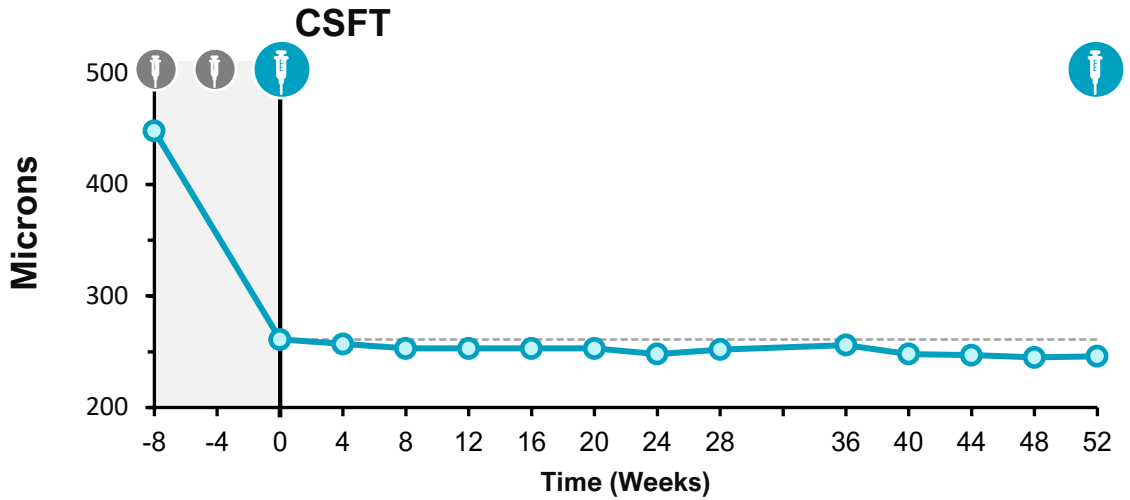
-8 Weeks	**BCVA:** 75 Ltrs **CSFT:** 344 µm	
Baseline	**BCVA:** 86 Ltrs *Snellen: 20/20* **CSFT:** 247 µm	
Week 4	**BCVA (Δ):** 84 (-2) Ltrs **CSFT (Δ):** 254 (+7) µm	
Week 12	**BCVA (Δ):** 85 (-1) Ltrs **CSFT (Δ):** 262 (+15) µm	
Week 24	**BCVA (Δ):** 80 (-6) Ltrs **CSFT (Δ):** 277 (+30) µm	
Week 36	**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

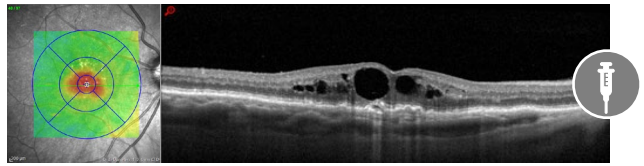
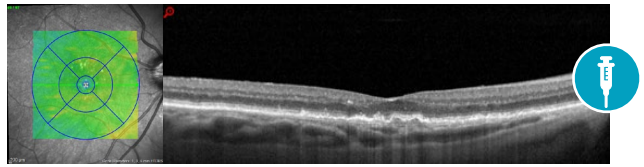
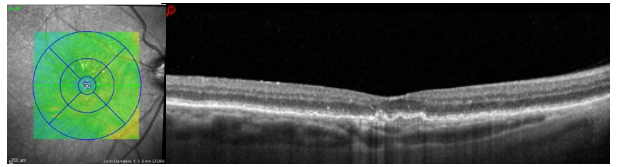
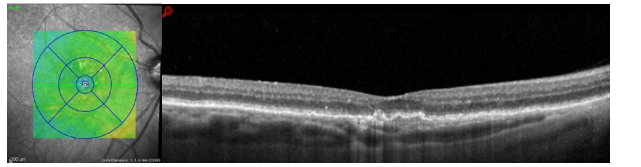
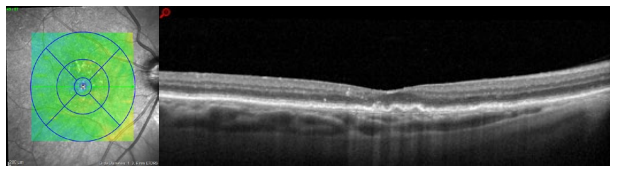
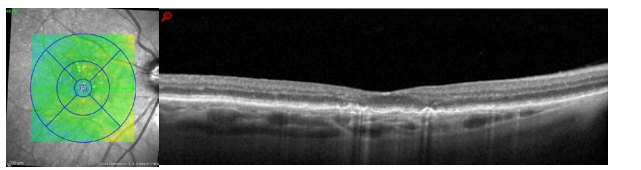
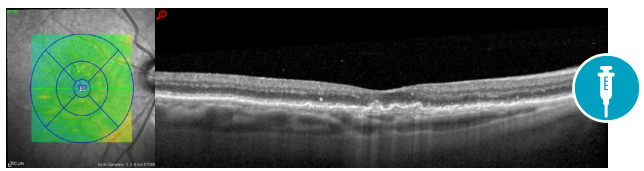
OTX-TKI Case 3





Screening
Aflibercept (2mg)

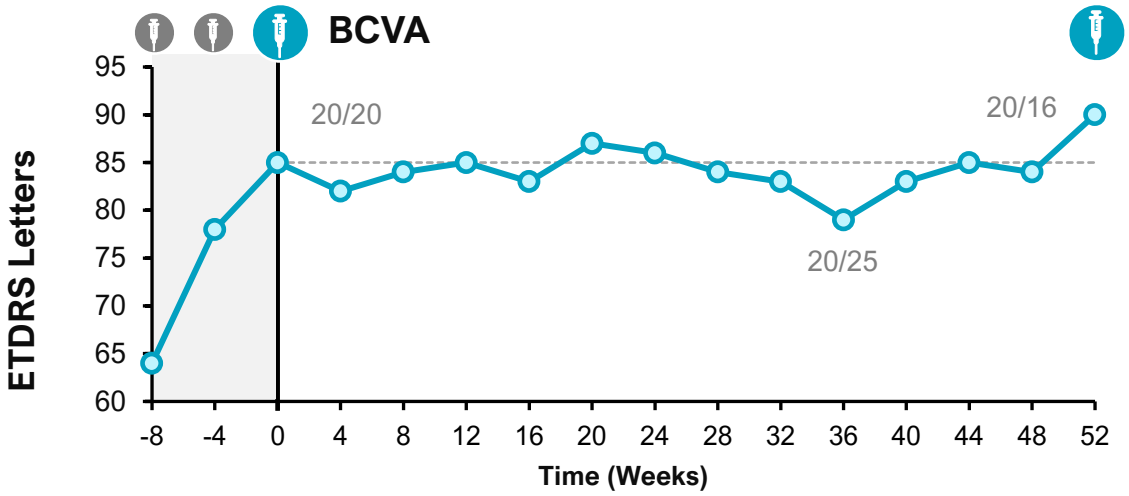
OTX-TKI
(0.45mg)

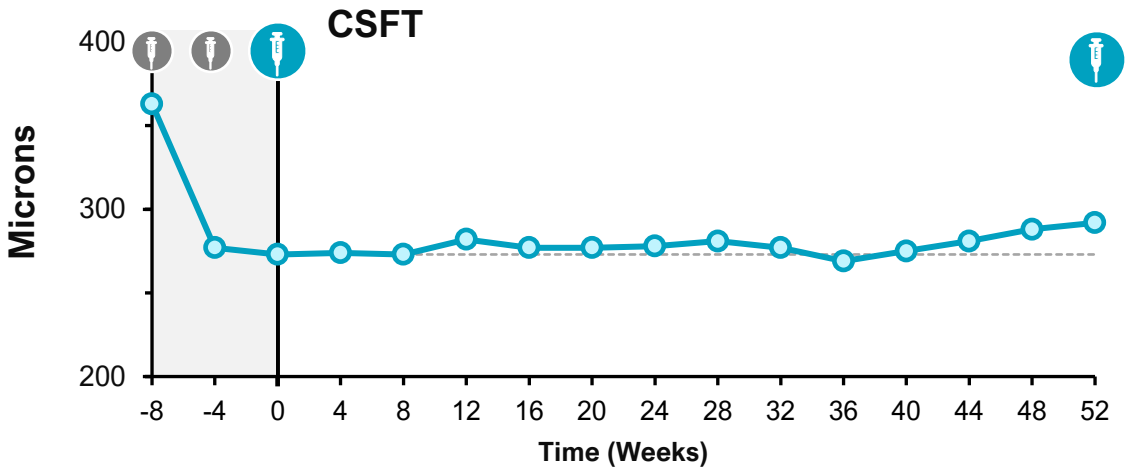
-8 Weeks	**BCVA:** 74 Ltrs **CSFT:** 448 µm	
Baseline	**BCVA:** 85 Ltrs *Snellen: 20/20* **CSFT:** 261 µm	
Week 4	**BCVA (Δ):** 85 (0) Ltrs **CSFT (Δ):** 257 (-4) µm	
Week 12	**BCVA (Δ):** 84 (-1) Ltrs **CSFT (Δ):** 253 (-8) µm	
Week 24	**BCVA (Δ):** 85 (0) Ltrs **CSFT (Δ):** 248 (-13) µm	
Week 36	**BCVA (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

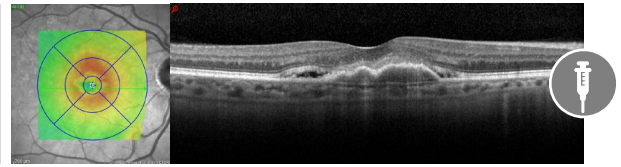
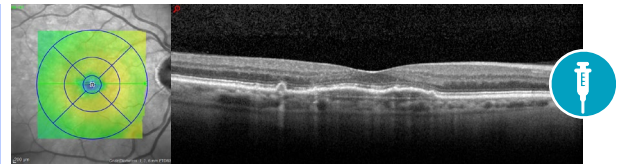
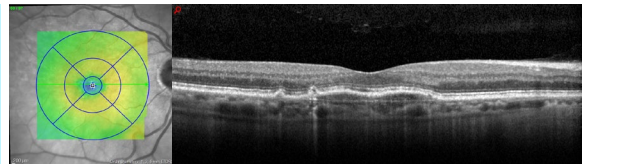
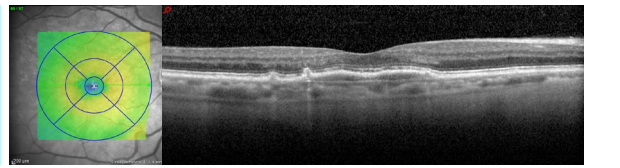
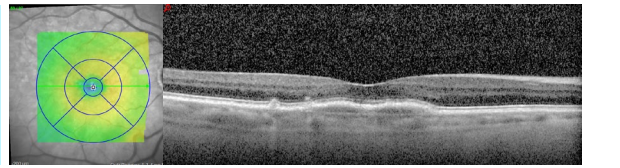
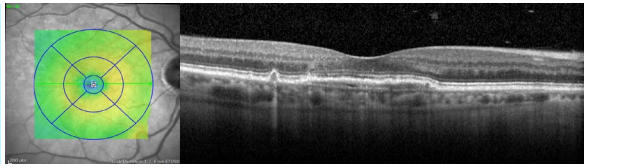
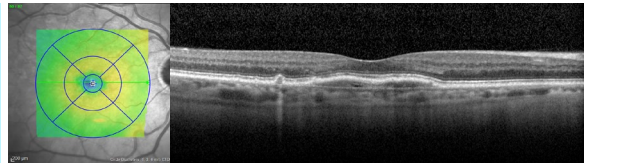
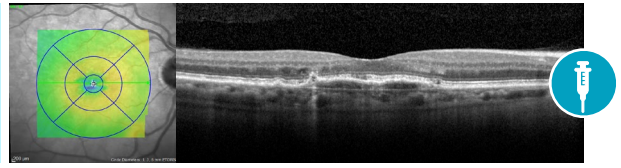
OTX-TKI Case 4





Screening
Aflibercept (2mg)

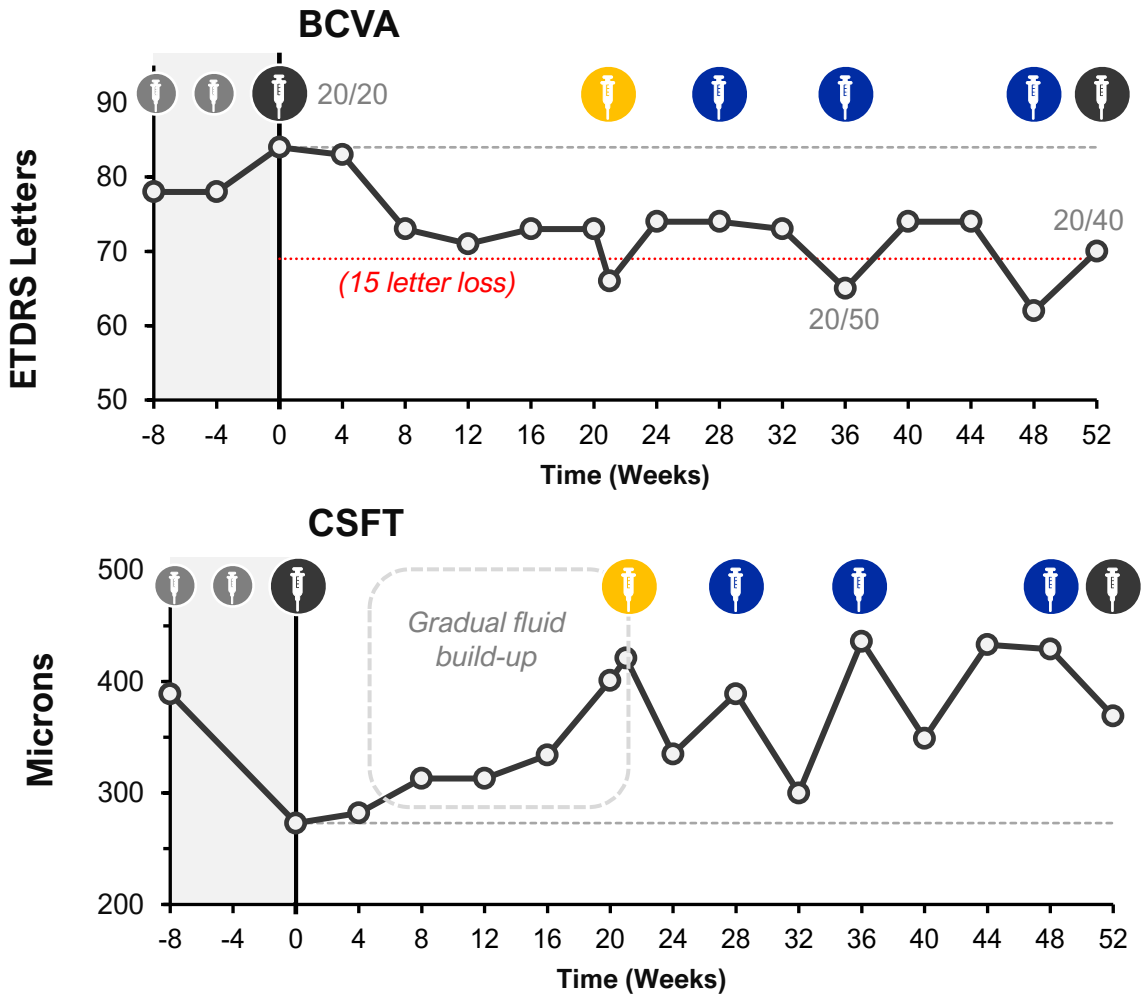
OTX-TKI
(0.45mg)

-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 2

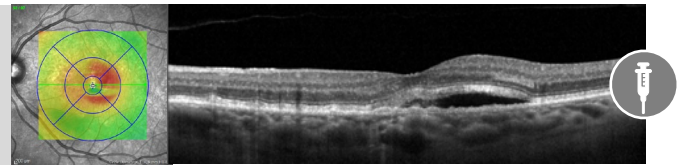
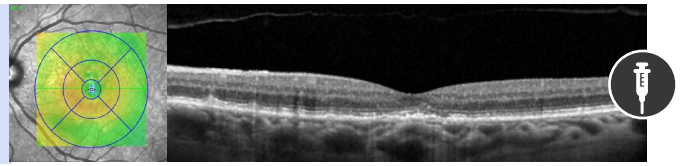
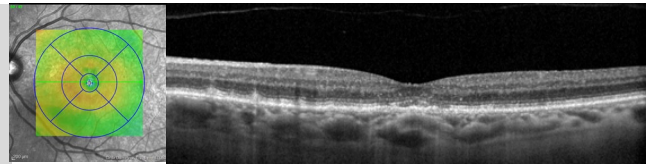
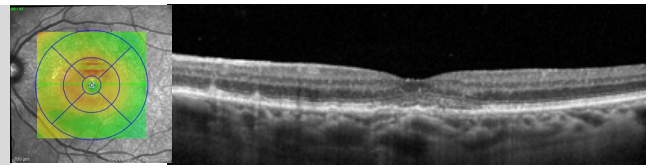
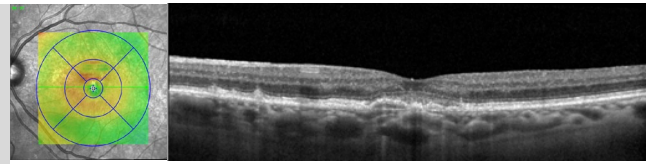
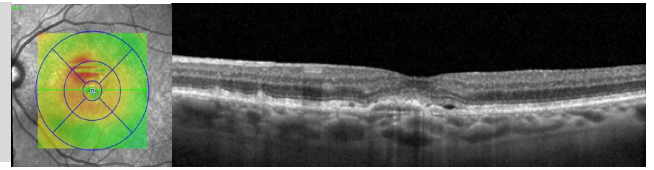
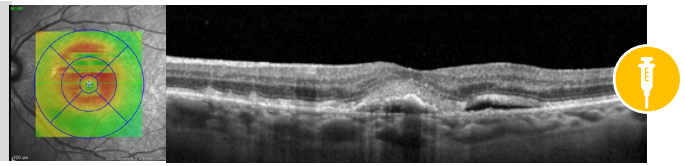


Screening Aflibercept (2mg)

Study Aflibercept (2 mg)

Per-Protocol Rescue Aflibercept (2mg)

Investigator Discretion Rescue

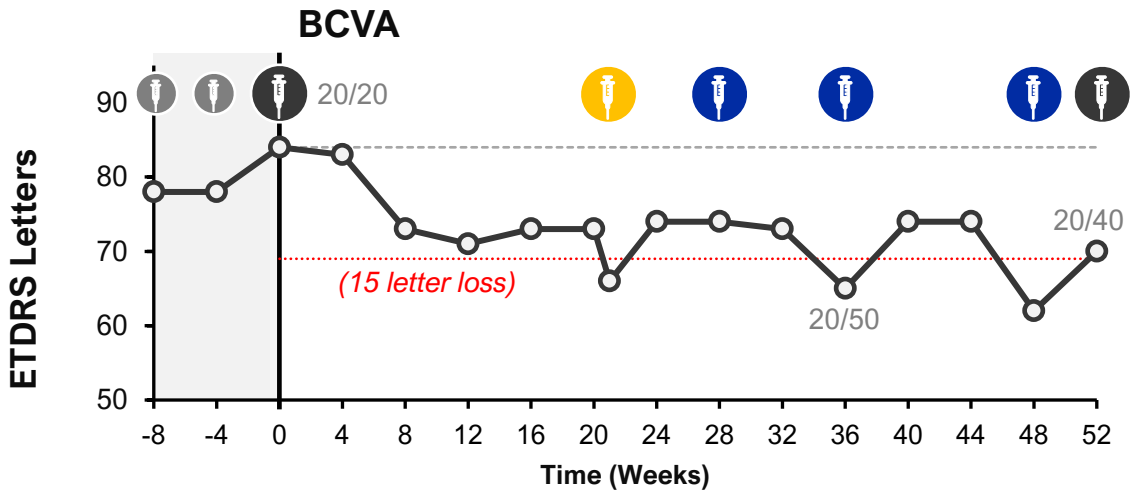
-8 Weeks	**BCVA:** 78 Ltrs **CSFT:** 389 µm	
Baseline	**BCVA:** 84 Ltrs *Snellen: 20/20* **CSFT:** 273 µm	
Week 4	**BCVA (Δ):** 83 (-1) Ltrs **CSFT (Δ):** 282 (+9) µm	
Week 8	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 313 (+40) µm	
Week 12	**BCVA (Δ):** 71 (-13) Ltrs **CSFT (Δ):** 313 (+40) µm	
Week 16	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 334 (+61) µm	
Week 21 *unscheduled*	**BCVA (Δ):** 66 (-18) Ltrs **CSFT (Δ):** 421 (+148) µm	

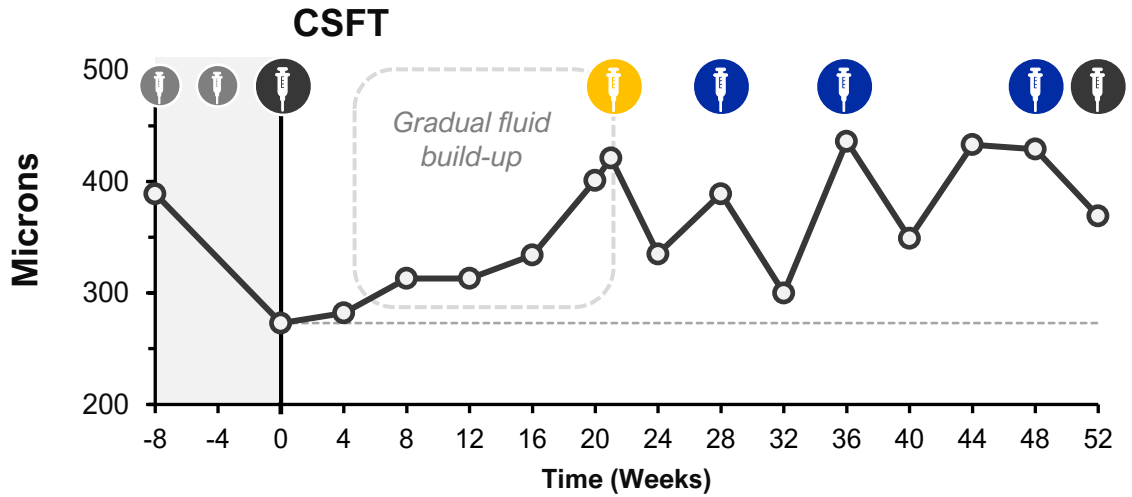
OCULAR THERAPEUTIX

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



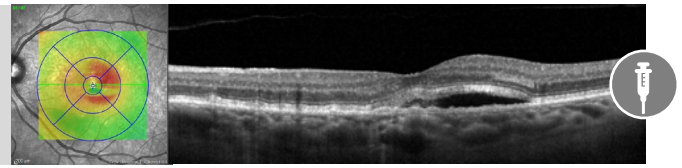
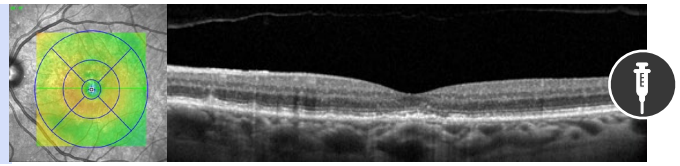
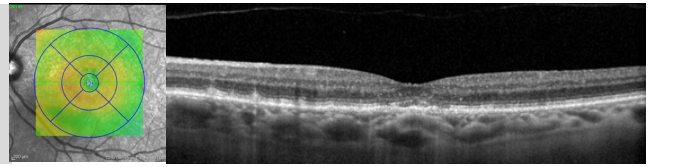
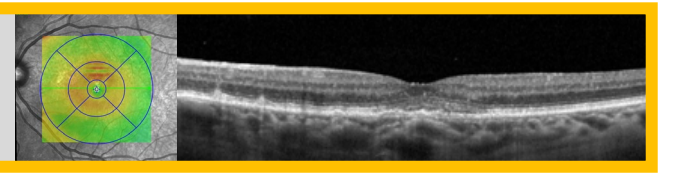
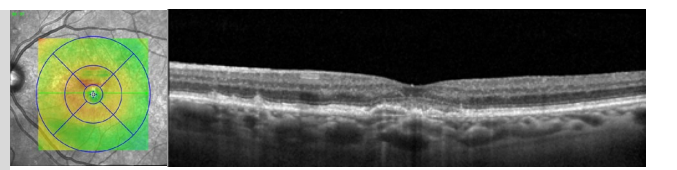
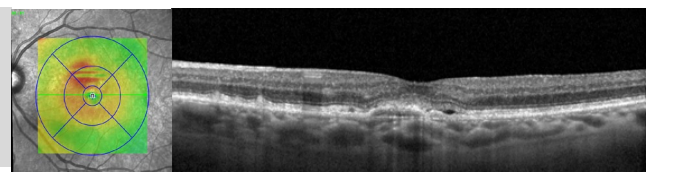
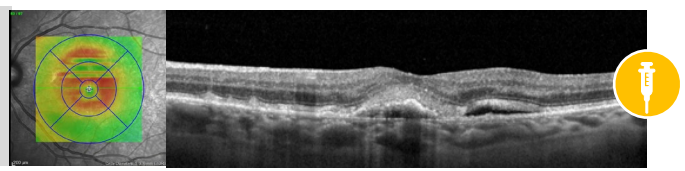


Screening Aflibercept (2mg)

Study Aflibercept (2 mg)

Per-Protocol Rescue Aflibercept (2mg)

Investigator Discretion Rescue

-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 12	**BCVA (Δ):** 71 (-13) 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	

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

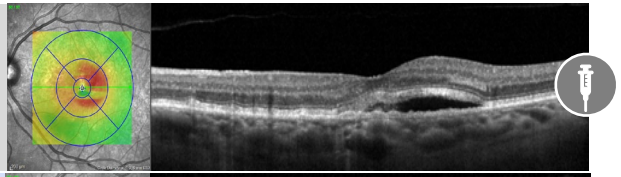
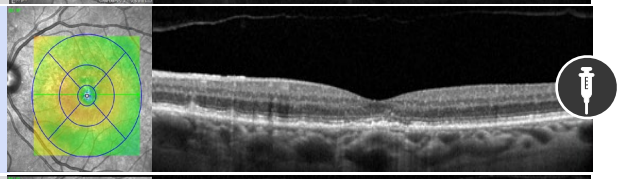
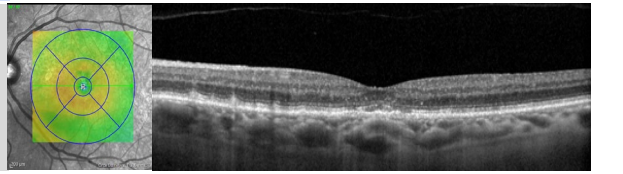
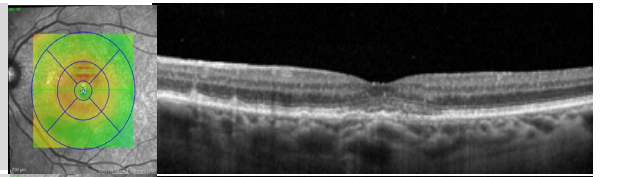
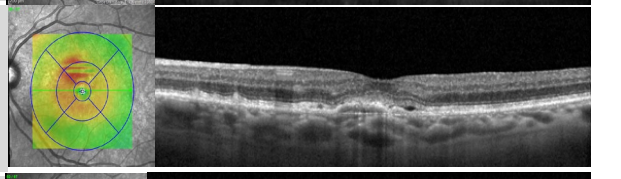
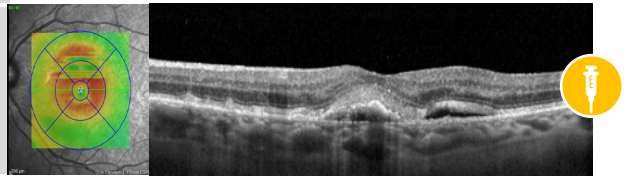
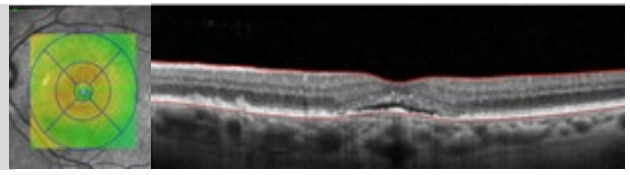
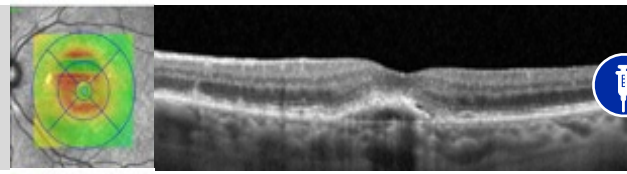
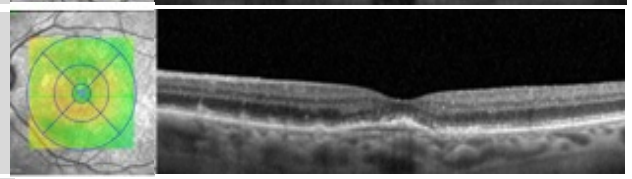
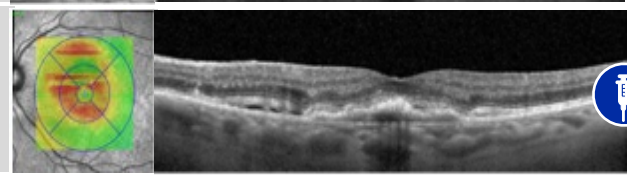
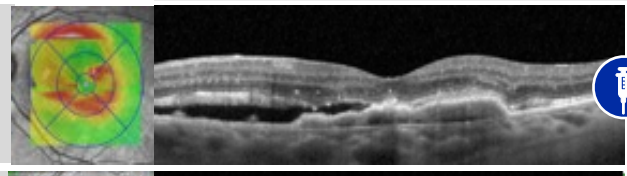
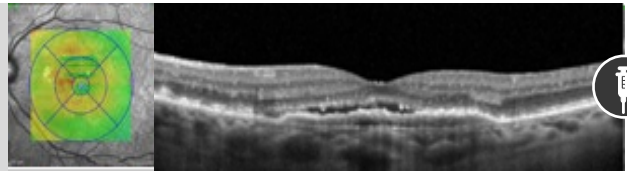
Aflibercept Case 2

Screening Aflibercept (2mg)

Study Aflibercept (2 mg)

Per-Protocol Rescue Aflibercept (2mg)

Investigator Discretion Rescue

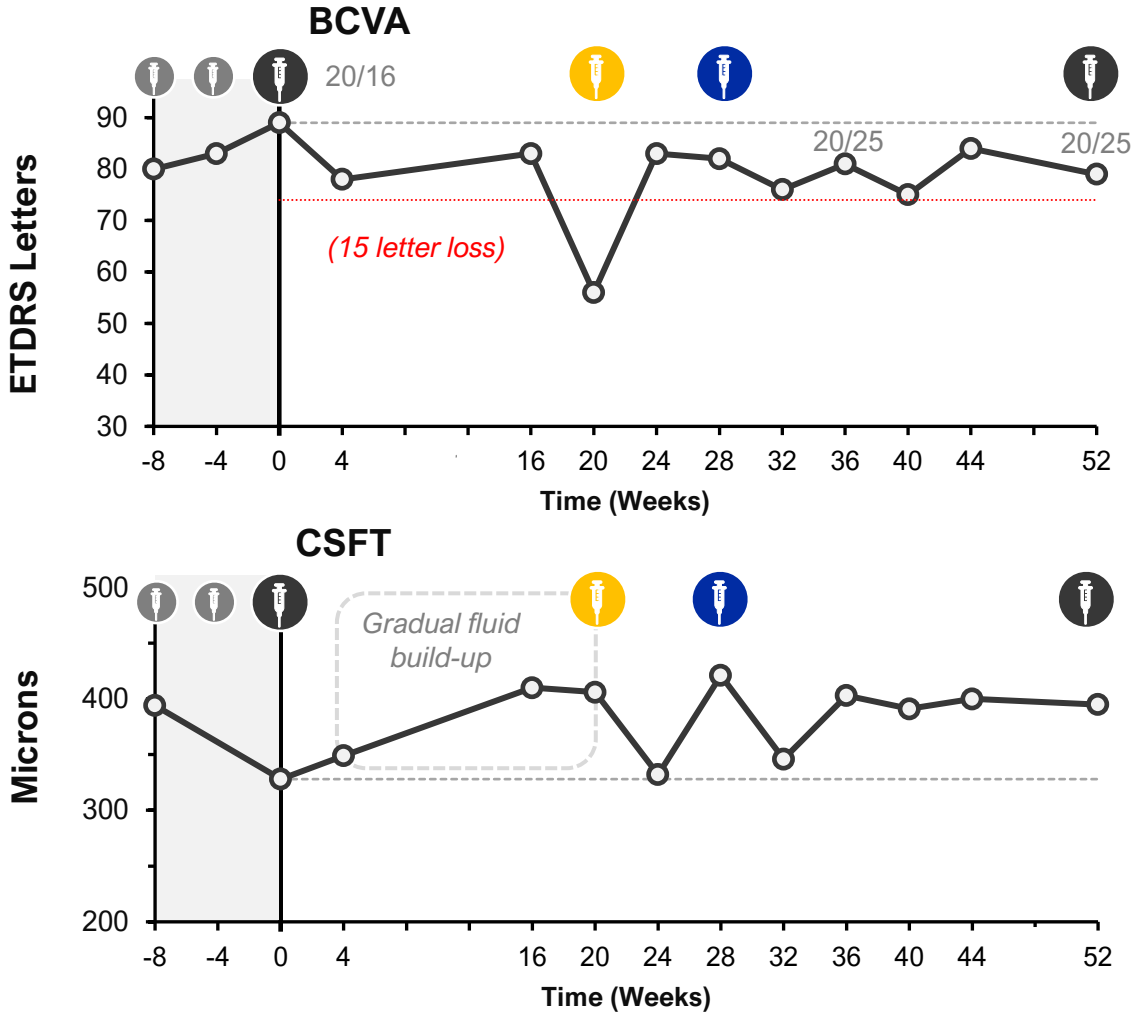
-8 Weeks	**BCVA:** 78 Ltrs **CSFT:** 389 µm	
Baseline	**BCVA:** 84 Ltrs *Snellen: 20/20* **CSFT:** 273 µm	
Week 4	**BCVA (Δ):** 83 (-1) Ltrs **CSFT (Δ):** 282 (+9) µm	
Week 8	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 313 (+40) µm	
Week 16	**BCVA (Δ):** 73 (-11) Ltrs **CSFT (Δ):** 334 (+61) µm	
Week 21 *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 3

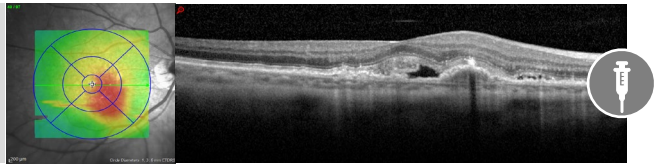
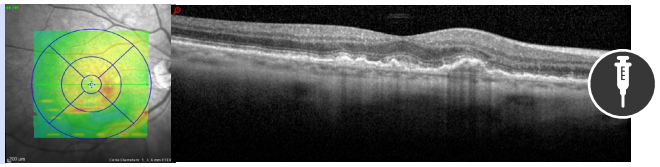
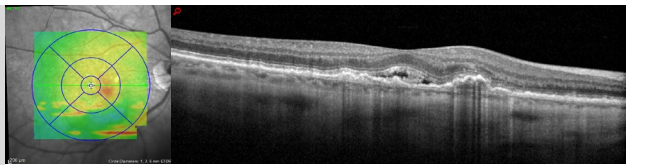
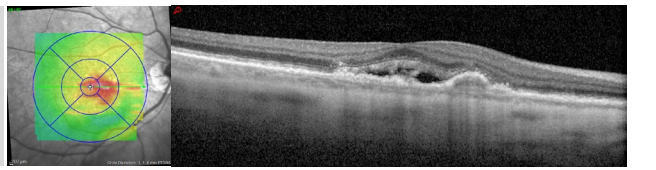
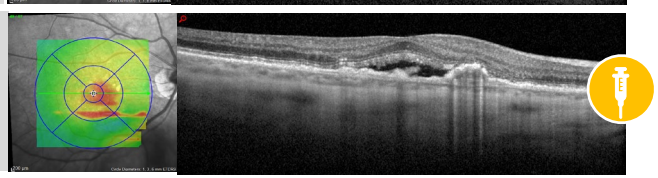
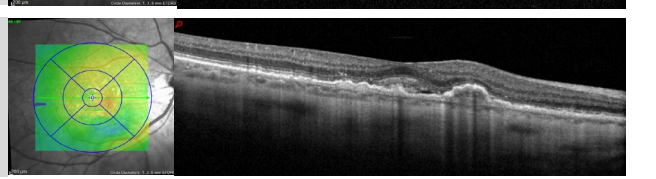
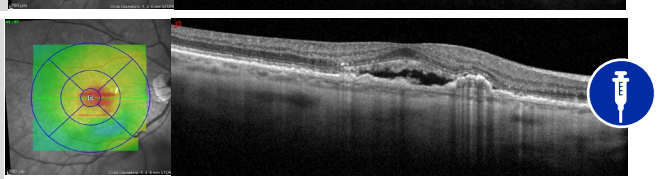
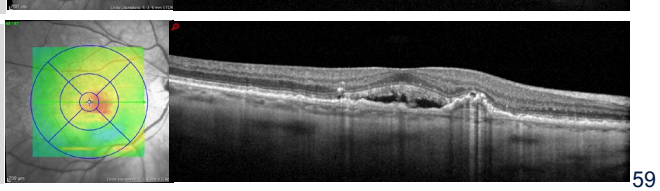


Screening Aflibercept (2mg)

Study Aflibercept (2 mg)

Per-Protocol Rescue Aflibercept (2mg)

Investigator Discretion Rescue

-8 Weeks	**BCVA:** 80 Ltrs **CSFT:** 394 µm	
Baseline	**BCVA:** 89 Ltrs *Snellen: 20/16* **CSFT:** 328 µm	
Week 4	**BCVA (Δ):** 78 (-11) Ltrs **CSFT (Δ):** 349 (+21) µm	
Week 16	**BCVA (Δ):** 83 (-6) Ltrs **CSFT (Δ):** 410 (+82) µm	
Week 20	**BCVA (Δ):** 56 **(-33)** Ltrs **CSFT (Δ):** 406 (+78) µm	
Week 24	**BCVA (Δ):** 83 (-6) Ltrs **CSFT (Δ):** 332 (+4) µm	
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	

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

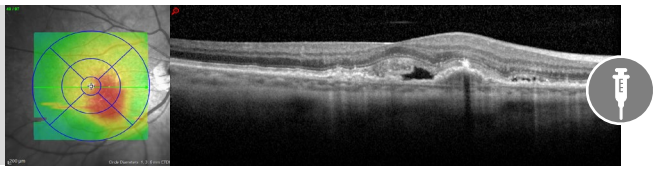
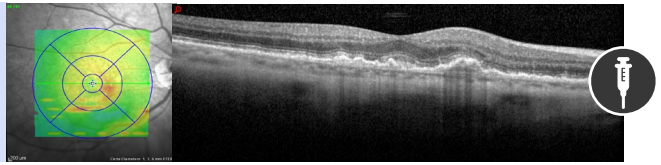
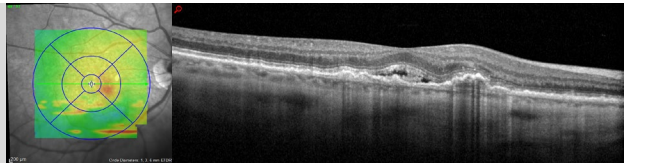
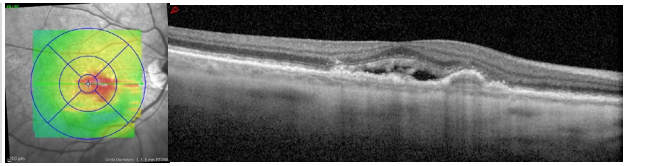
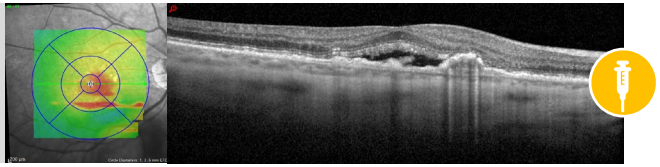
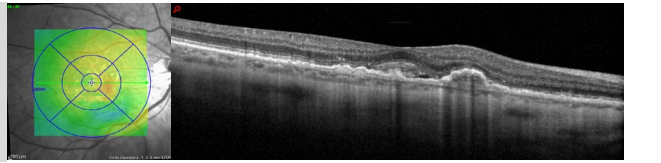
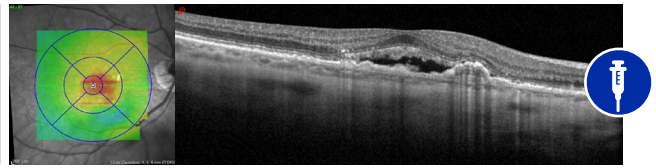
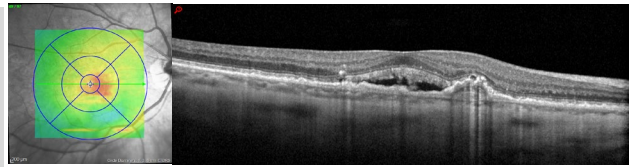
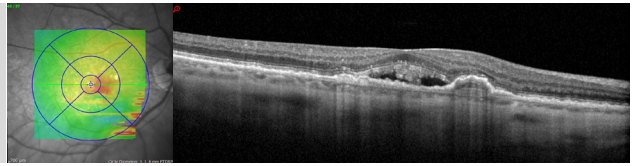
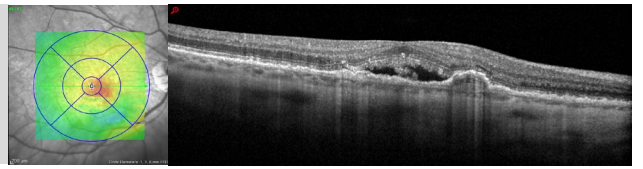
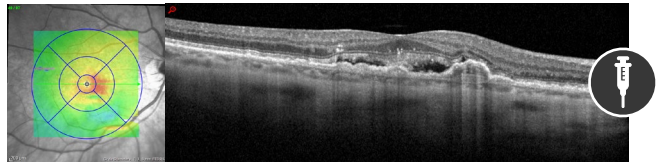
Aflibercept Case 3

Screening Aflibercept (2mg) injection

Study Aflibercept (2 mg) administration

Per-Protocol Rescue Aflibercept (2mg)

Investigator Discretion Rescue

-8 Weeks	**BCVA:** 80 Ltrs **CSFT:** 394 µm	
Baseline	**BCVA:** 89 Ltrs *Snellen: 20/16* **CSFT:** 328 µm	
Week 4	**BCVA (Δ):** 78 (-11) Ltrs **CSFT (Δ):** 349 (+21) µm	
Week 16	**BCVA (Δ):** 83 (-6) Ltrs **CSFT (Δ):** 410 (+82) µm	
Week 20	**BCVA (Δ):** 56 (-33) Ltrs **CSFT (Δ):** 406 (+78) µm	
Week 24	**BCVA (Δ):** 83 (-6) Ltrs **CSFT (Δ):** 332 (+4) µm	
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	
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

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

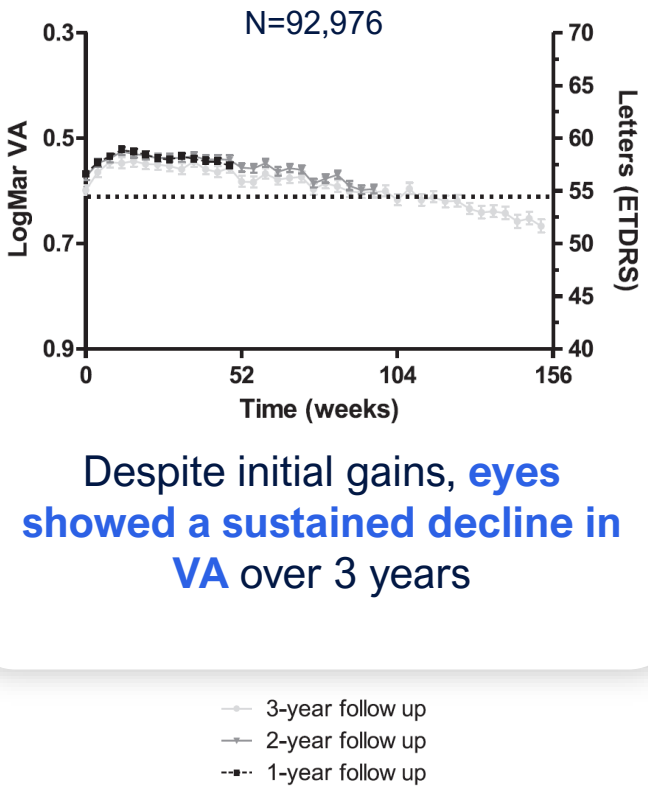
Key Insights

Mark R. Barakat, MD

OCULAR THERAPEUTIX Retina experience redefined

Eyes with Excellent Baseline Vision Decline on Average in Real-World Studies

Visual Acuity Over Time



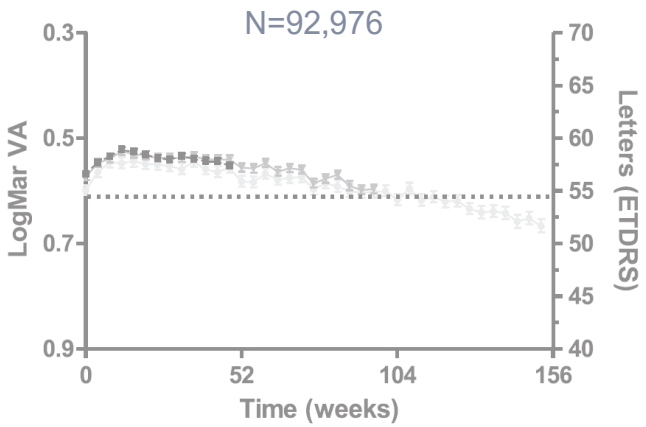
Despite initial gains, **eyes showed a sustained decline in VA** over 3 years

OCULAR THERAPEUTIX Retina experience redefined™

Writing Committee for the UK Age-Related Macular Degeneration EMR Users Group. The neovascular age-related macular degeneration database: multicenter study of 92 976 ranibizumab injections: report 1: visual acuity. *Ophthalmology*. 2014;121(5):1092-1101.
ETDRS, Early Treatment Diabetic Retinopathy Study; VA, visual acuity; RWE, real world evidence

Eyes with Excellent Baseline Vision Decline on Average in Real-World Studies

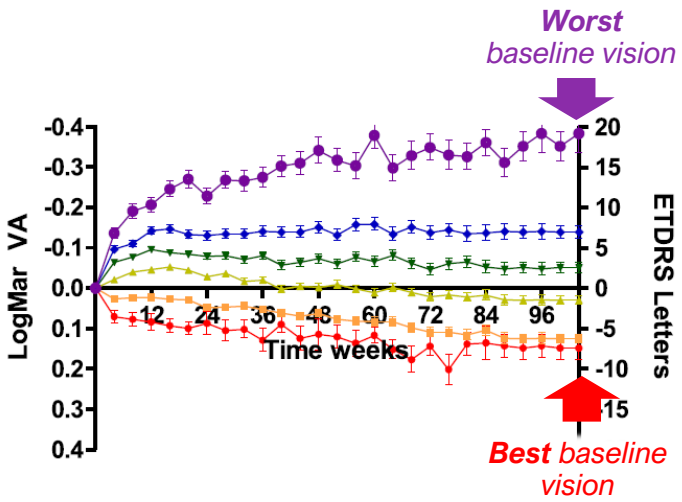
Visual Acuity Over Time



Despite initial gains, **eyes showed a sustained decline in VA** over 3 years

3-year follow up
2-year follow up
1-year follow up

Change in Vision
Stratified by Baseline VA



Change in vision is dependent on baseline status with **eyes starting with better vision showing greater decline**

Baseline -0.29-0.00 (n=166)
Baseline 0.01-0.30 (n=2166)
Baseline 0.31-0.60 (n=3729)
Baseline 0.61-0.90 (n=2905)
Baseline 0.91-1.20 (n=1843)
Baseline 1.21-1.50 (n=411)

OCULAR THERAPEUTIX Retina experience redefined™

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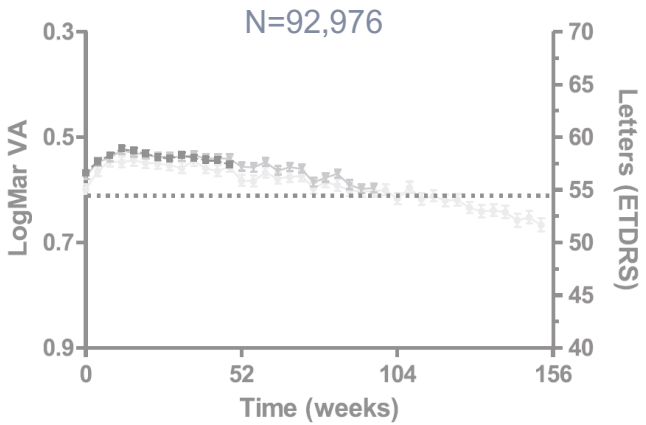
ETDRS, Early Treatment Diabetic Retinopathy Study; VA, visual acuity; RWE, real world evidence

Actual Visual Acuity, NOT Change, is What is Meaningful to Patients

Visual Acuity Over Time



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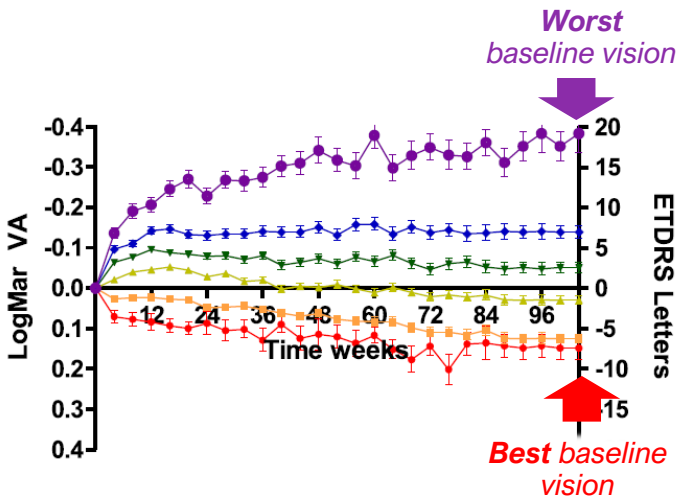

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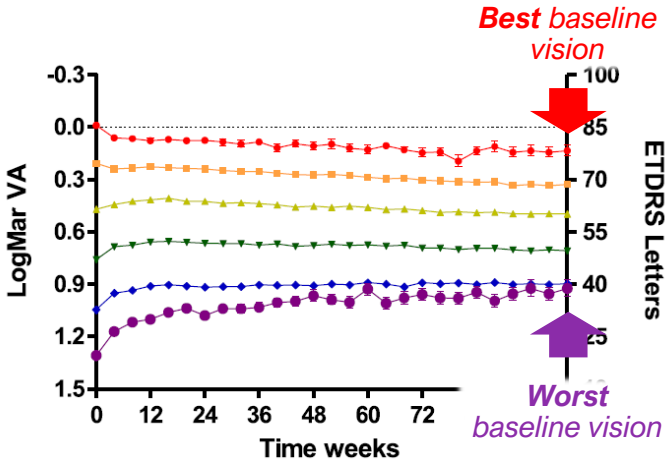
Mean Vision
Stratified by Baseline VA



Best baseline vision maintains the highest overall visual acuity

Baseline -0.29-0.00 (n=166)
Baseline 0.01-0.30 (n=2166)
Baseline 0.31-0.60 (n=3729)
Baseline 0.61-0.90 (n=2905)
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OCULAR THERAPEUTIX Retina experience redefined™

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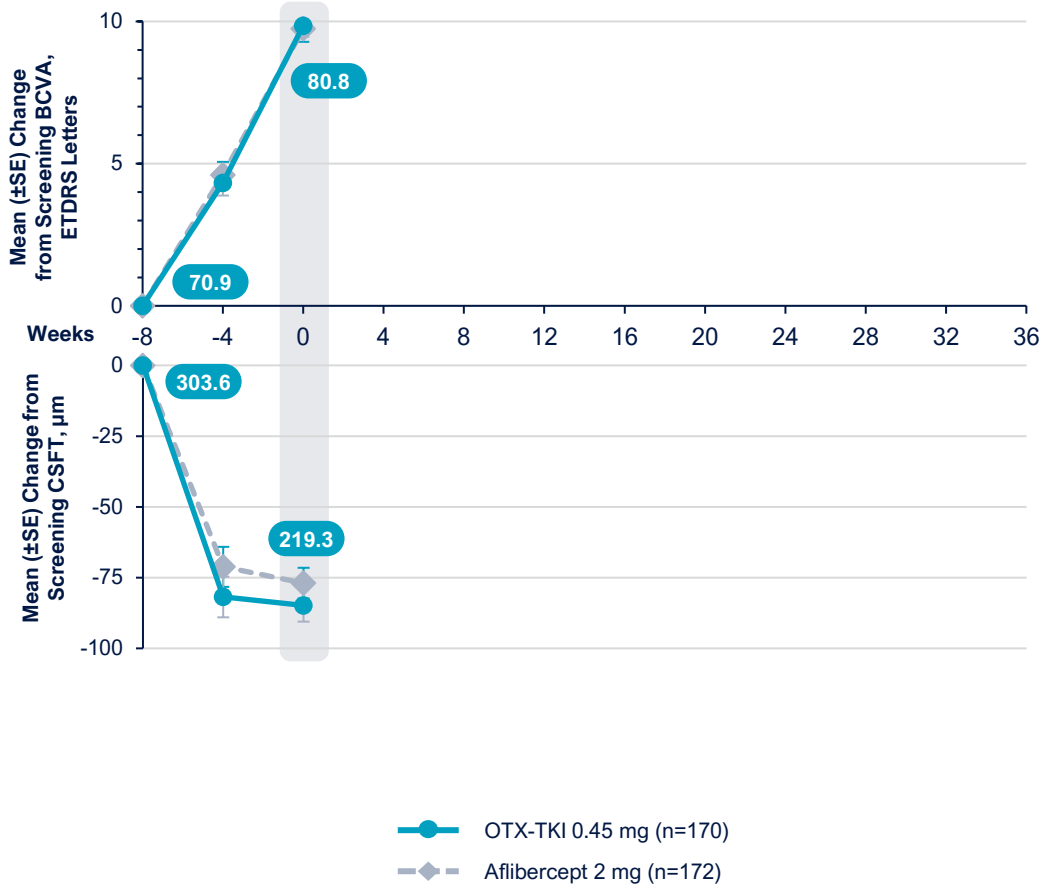
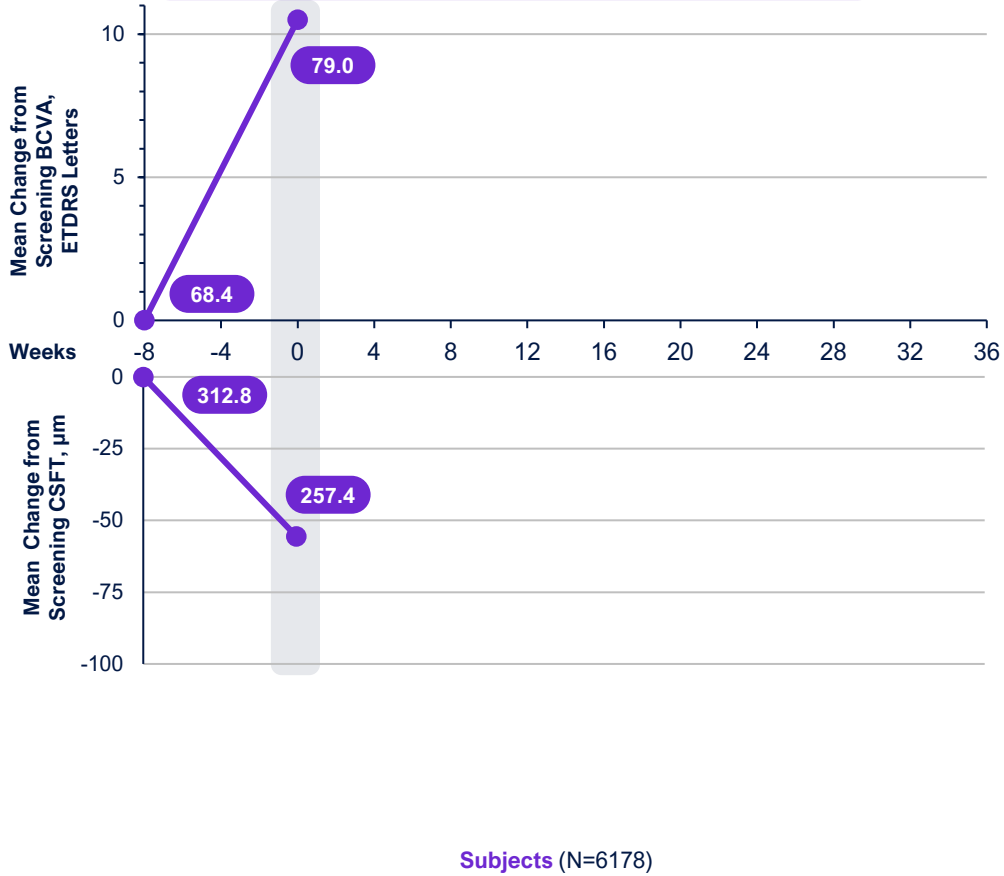
How Does SOL-1 Data Align with Real World Outcomes?

SOL-1 Clinical Trial
Post Hoc Analysis



SOL-1 Emulated Population
IRIS Registry



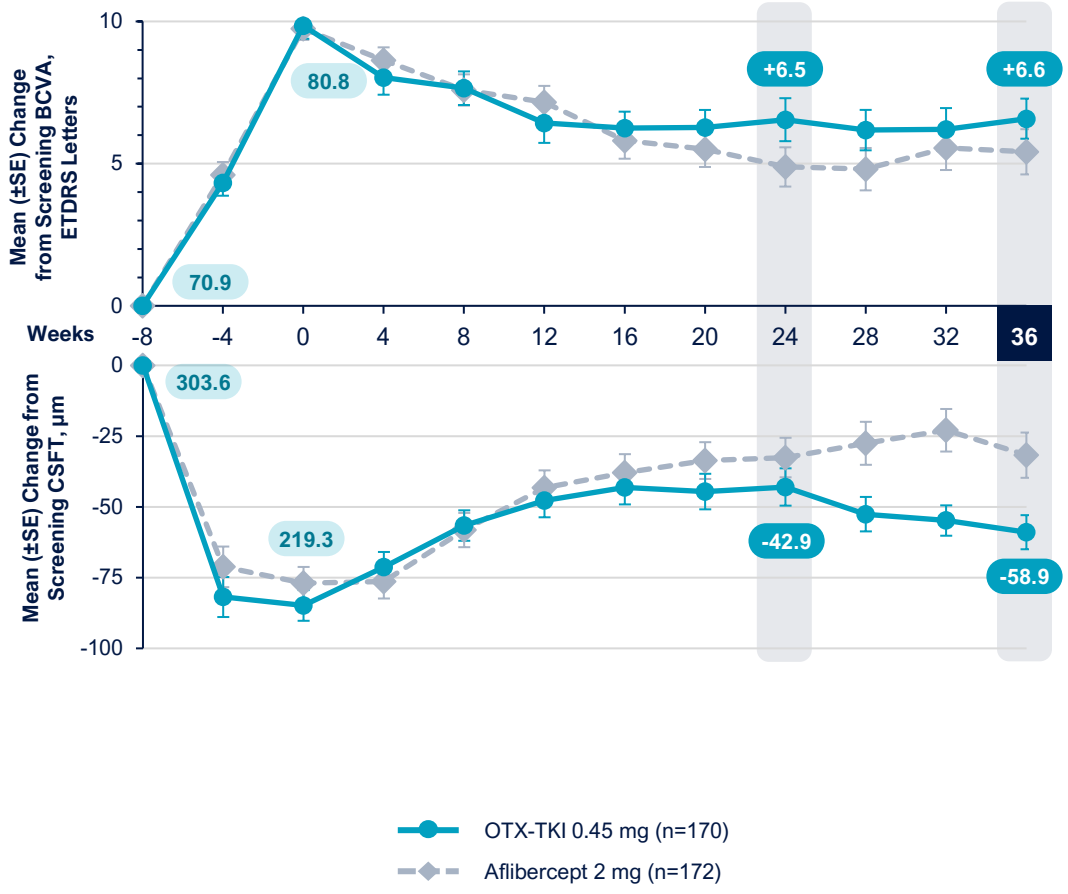
Subjects (N=6178)

OCULAR THERAPEUTIX Retina experience redefined™

Data on File. Ocular Therapeutix. 2026

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

SOL-1 Clinical Trial
Post Hoc Analysis



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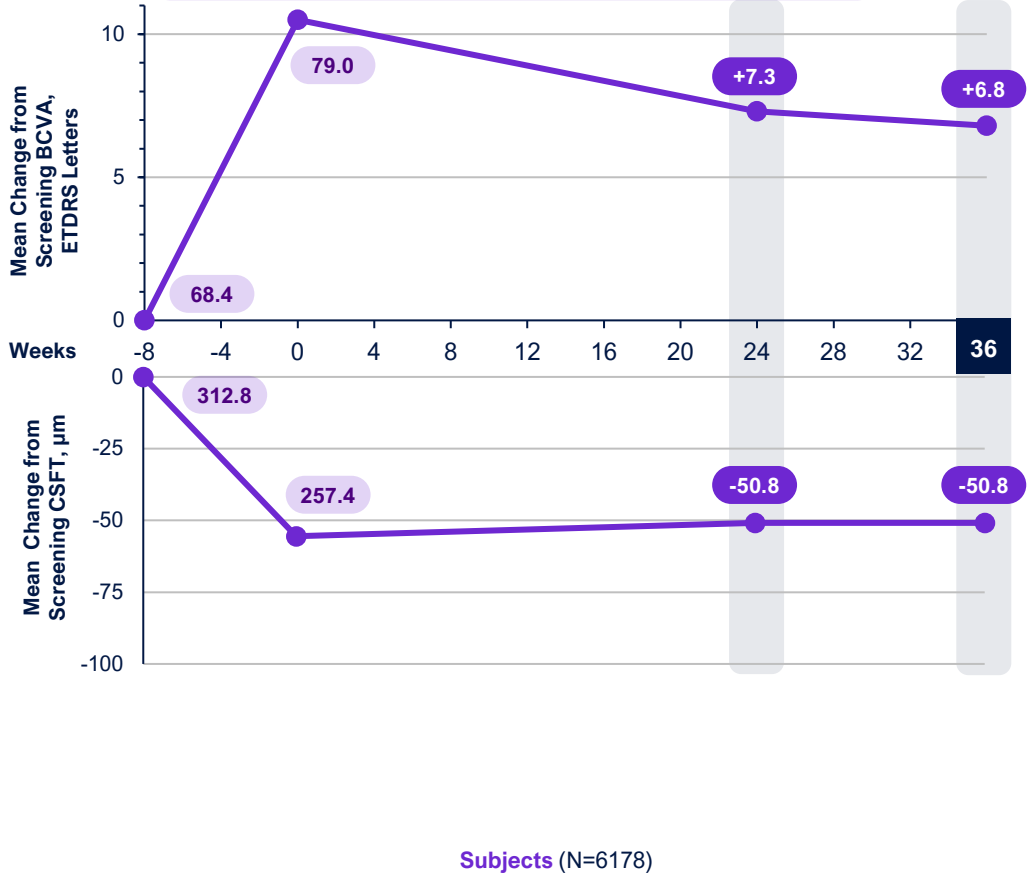

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OCULAR THERAPEUTIX Retina experience redefined™

Data on File. Ocular Therapeutix. 2026

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

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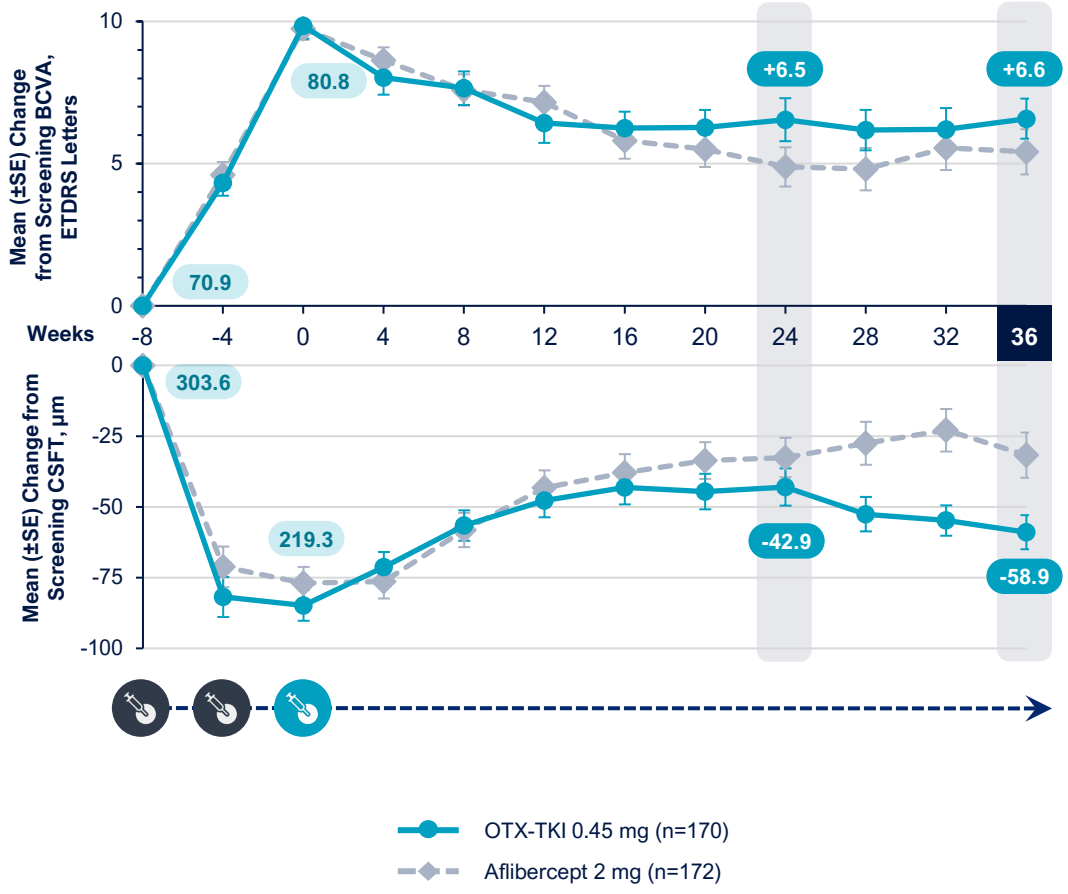

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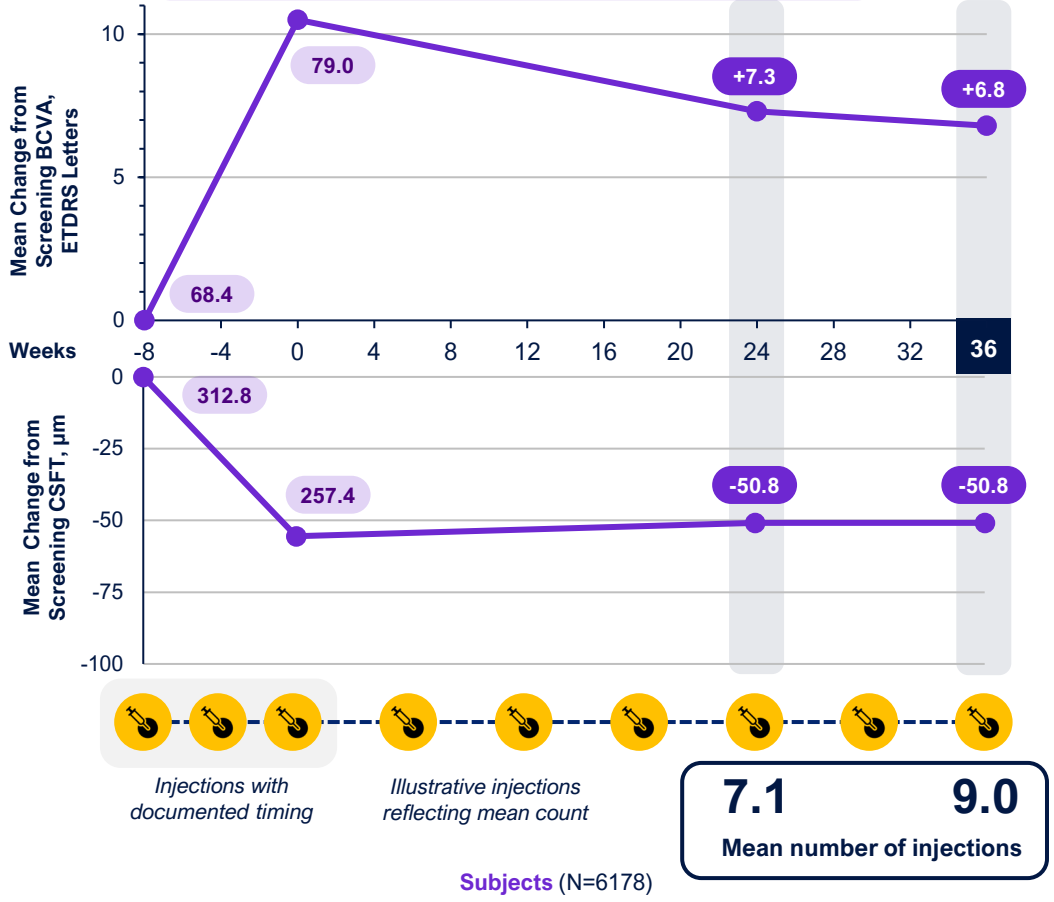


Data on File. Ocular Therapeutix. 2026

Clinical Program Update

Arshad M. Khanani, MD

OCULAR THERAPEUTIX Retina experience redefined

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

3Q 2026 — **Pre-NDA meeting:**
To align on format and content of information to be submitted in NDA

4Q 2026 — **SOL-R interim safety database lock** to reach >300 patients planned

4Q 2026 — **Complete 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

SOL: OTX-TKI Phase 3 Clinical Program in nAMD

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

Registrational Trials

Extension Study

SOL-1

Phase 3
Superiority Trial

Durability of a single OTX-TKI injection

SOL-R

Phase 3
Non-Inferiority Trial

Repeat dosing every 6 months

SOL-X

Open-Label Extension

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

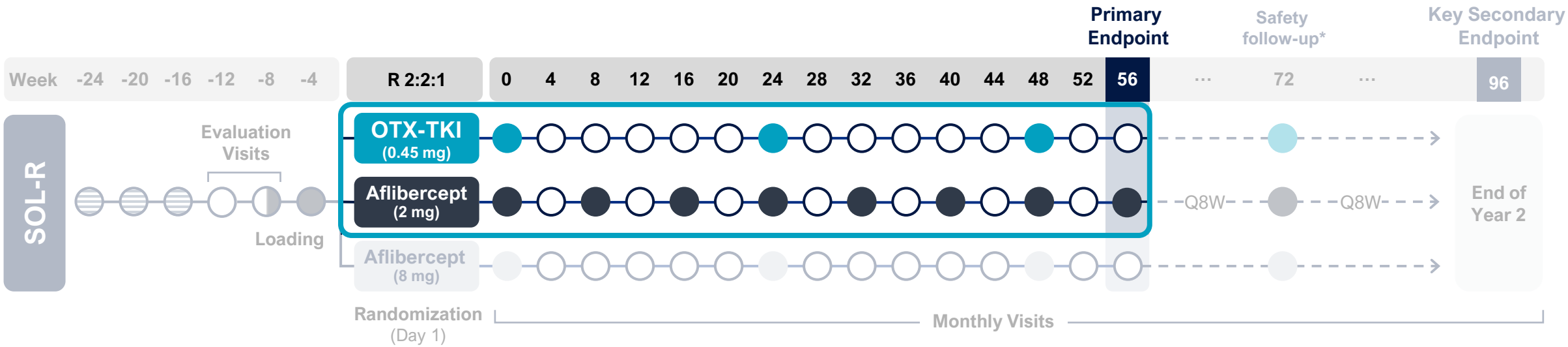
Eligible patients who complete end of Year 2 visit in SOL-1 or SOL-R

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

SOL-R Design: Updates & Considerations



FDA Guidance for Non-Inferiority Trials

Compare to labeled dosing of Aflibercept 2 mg or Ranibizumab 0.5 mg **(-4.5 letter margin)**[1]

SOL-R Trial Design

Primary analysis: OTX-TKI dosed Q24W versus Aflibercept 2mg Q8W

Screening Dose, Any Anti VEGF† | 2nd evaluation & Aflibercept 2mg | OTX-TKI 0.45mg | Aflibercept 2 mg | Aflibercept 8 mg | Study visit

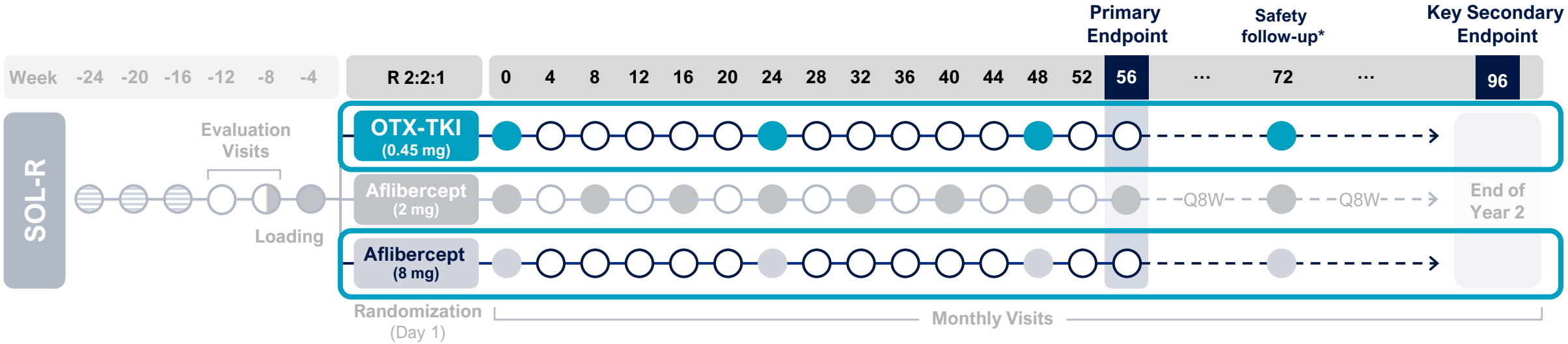
OCULAR THERAPEUTIX Retina experience redefined™

ClinicalTrials.gov identifier: NCT06495918

1. U.S. Food and Drug Administration. Neovascular AMD: Developing Drugs for Treatment Guidance for Industry. 2023

Q24W, every 24 weeks; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor; † Any anti-VEGF except Beovu

SOL-R Design: Updates & Considerations



FDA Guidance for Wet AMD Trials

One comparator arm should have the same dosing schedule as the investigational drug[1]

SOL-R Trial Design

Aflibercept 8mg dosing identical with key secondary endpoint at week 96

Screening Dose, Any Anti VEGF† | 2nd evaluation & Aflibercept 2mg | OTX-TKI 0.45mg | Aflibercept 2 mg | Aflibercept 8 mg | Study visit

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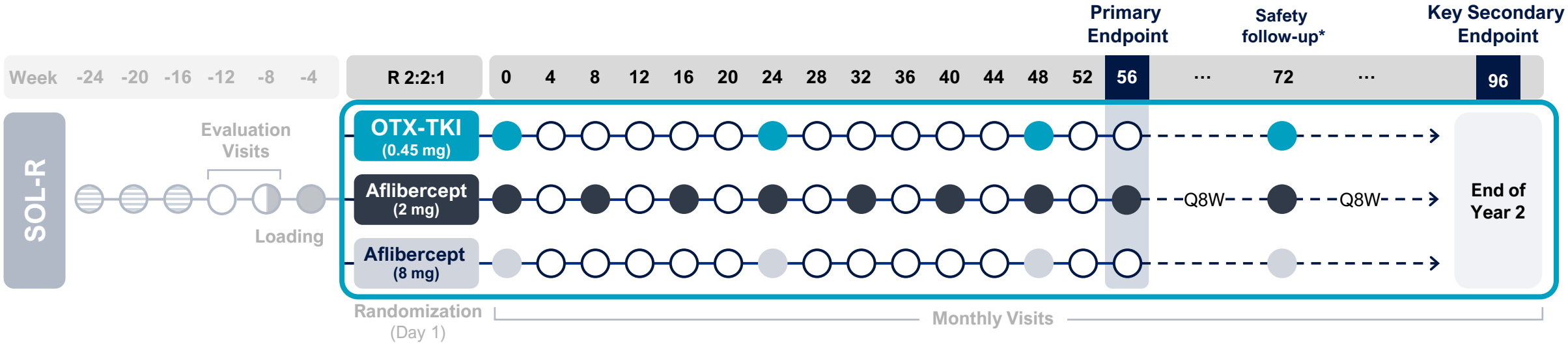
SOL-R Design: Updates & Considerations



FDA Guidance for Wet AMD Trials

Sham injections are not recommended
due to inadequate masking[1,2]

SOL-R Trial Design

No sham injections

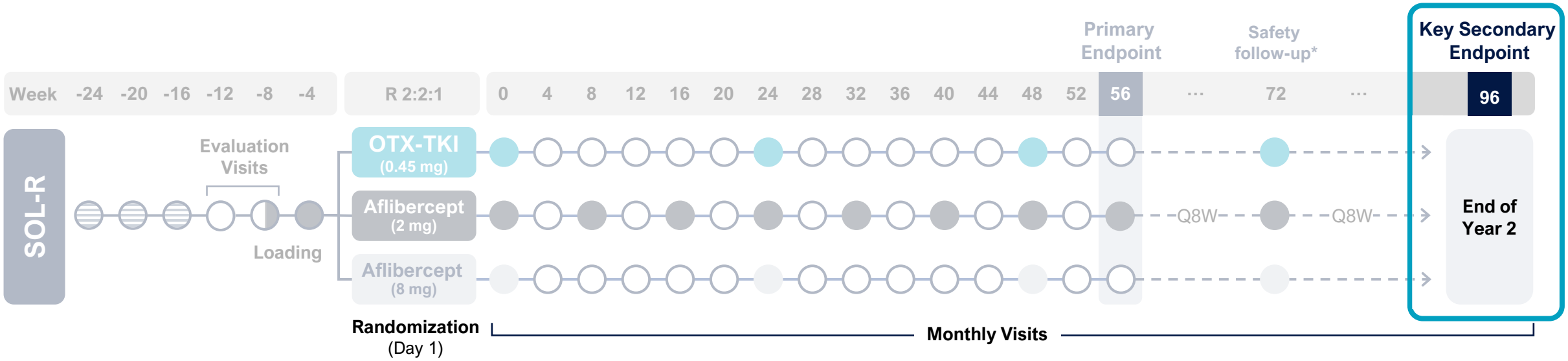
Screening Dose, Any Anti VEGF† | 2nd evaluation & Aflibercept 2mg | OTX-TKI 0.45mg | Aflibercept 2 mg | Aflibercept 8 mg | Study visit

OCULAR THERAPEUTIX Retina experience redefined™

ClinicalTrials.gov identifier: NCT06495918

1. Type C WRO [written response only] Aug 2024. 2. Weiss J, Boyd B, Event: Q&A with FDA, at the American Academy of Ophthalmology Annual Meeting, October 20, 2024
AMD, age-related macular degeneration; Q8W, every 8 weeks; VEGF, vascular endothelial growth factor; † Any anti-VEGF except Beovu

SOL-R Design: Updates & Considerations



SOL-R Year 1 Efficacy No Longer Part of OTX-TKI NDA Review

New Plan to Maintain Masking until Week 96 OTX-TKI Secondary Endpoints

vs. aflibercept (8 mg)

Key Secondary Endpoint:
Superiority comparison at Year 2

vs. aflibercept (2 mg)

Secondary Endpoint: Evaluating prevention of fibrosis and atrophy

Screening Dose, Any Anti VEGF† | 2nd evaluation & Aflibercept 2mg | OTX-TKI 0.45mg | Aflibercept 2 mg | Aflibercept 8 mg | Study visit

OCULAR THERAPEUTIX Retina experience redefined™

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Extension Study

SOL-1

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Superiority Trial

Durability of a single OTX-TKI injection

SOL-R

Phase 3
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Eligible patients who complete end of Year 2 visit in SOL-1 or SOL-R

OCULAR THERAPEUTIX Retina experience redefined™

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

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)

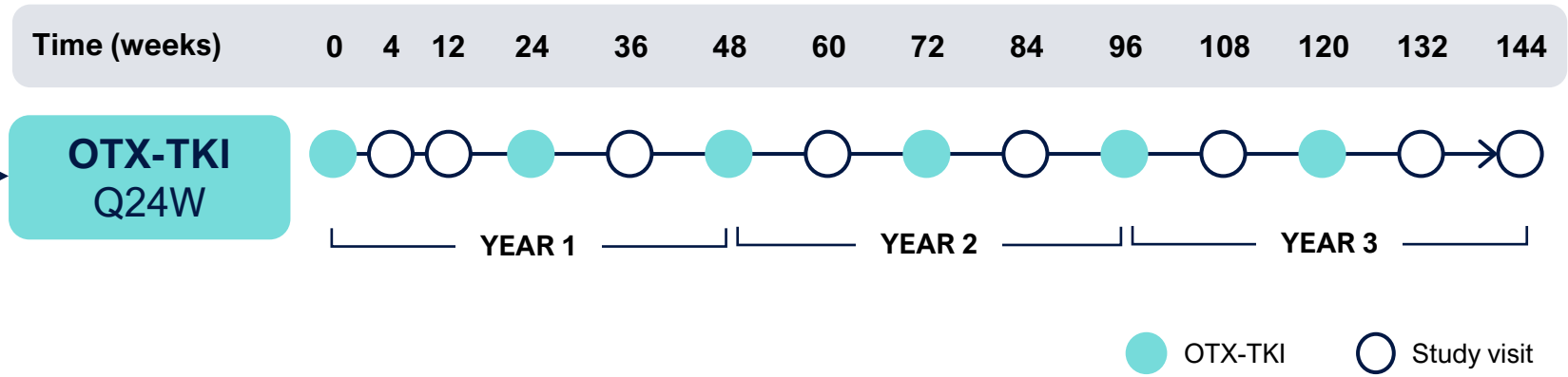
SOL-R

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

SOL-X

Three-year additional follow-up

OTX-TKI Q24W



OCULAR THERAPEUTIX Retina experience redefined

ClinicalTrials.gov Identifier: NCT07516132
Q24W, every 24 weeks

Streamlining Diabetic Retinopathy Program

Updated HELIOS-3 Study Design

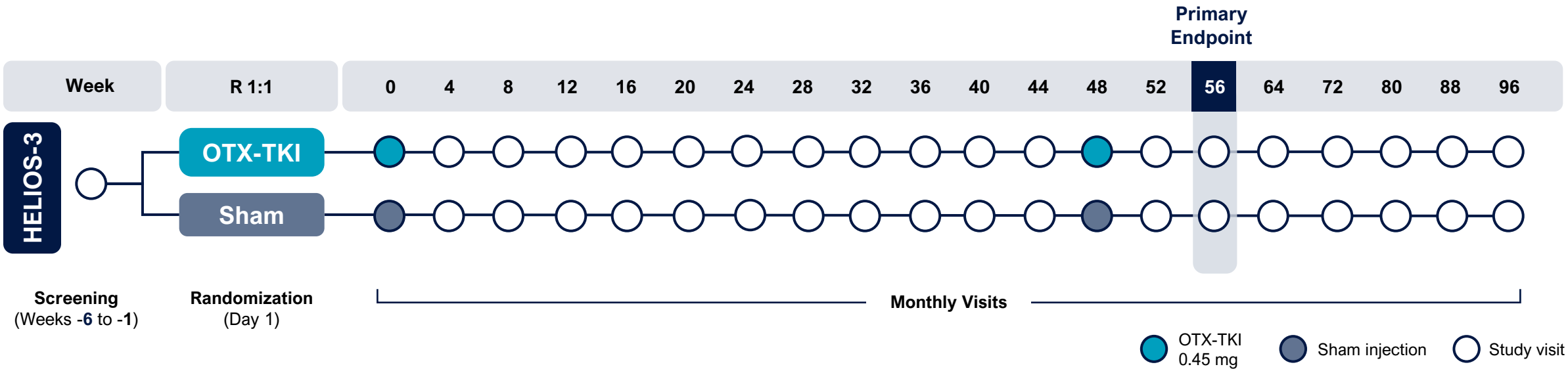
- Evaluation of only Q12M OTX-TKI regimen vs Sham
- Prioritizing One DR Registrational Trial (HELIOS-3)

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)



ClinicalTrials.gov Identifier: NCT07235085
CI-DME, center involved diabetic macular edema; DR, diabetic retinopathy; NPDR, non-proliferative DR; DRSS, Diabetic Retinopathy Severity Score; Q12M, every 12 months

Redefining the Management of nAMD

The Impact of Durability and Sustained Disease Control

July 16, 2026

American Society of Retina Specialists | Montreal, Canada

OCULAR THERAPEUTIX

Retina experience redefined™

MC-US-OTX-0263

Panel Discussion

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