

Redefining the Management of nAMD

The Impact of Durability and Sustained Disease Control

October 10, 2026

American Academy of Ophthalmology | New Orleans, LA



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trial being conducted under a Special Protocol Assessment (SPA) agreement with the U.S. FDA and aligned with FDA draft guidance for neovascular AMD drug development; the timing, design, enrollment, randomization, conduct and retention of subjects in the Company's clinical trials,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

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

Faculty



Mark R. Barakat
MD, FASRS

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



Dilsher S. Dhoot
MD, FASRS

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



Arshad M. Khanani
MD, MA, FASRS

Managing Partner, Director of
Clinical Research, Director of
Fellowship at Sierra Eye
Associates, and Clinical Associate
Professor at University of Nevada,
Reno, NV, USA

Disclosures

Mark R. Barakat

- **Consultant:** AbbVie Inc, Adverum, Alcon, Alkermes, Annexon Biosciences, Apellis, Astellas, Bausch and Lomb, Beacon, Biocryst, Boehringer Ingelheim, Celltrion, Cencora, Ceryvyn, Clearside, Eyepoint Pharma, Genentech, Glaukos, Harrow, Janssen, Kodiak Sciences, Ocular Therapeutix, Oculis, Outlook Therapeutics, Palatin Technologies, Regeneron, RegenxBio, RevOpsis Therapeutics, Roche, Sanofi, Stealth Biotherapeutics, Surrozen
- **Research Support:** 4DMT, Adverum, Annexon Biosciences, Astellas, Beacon, Boehringer Ingelheim, Ceryvyn, Clearside, Eyebio, Eyepoint Pharma, Genentech, Glaukos, Kanghong/Vanotech, Kodiak Sciences, Ocular Therapeutix, Oculis, Perfuse, Perceive Bio, Regeneron, RegenxBio, Sanofi, Stealth Biotherapeutics
- **Speaker:** Alcon, ANI Pharmaceuticals, Apellis, Astellas, Genentech, Regeneron,
- **Stock/Stock Options:** NeuBase, Oxurion, RevOpsisTherapeutics

Dilsher S. Dhoot

- **Consultant:** 4DMT, Abbvie, Adverum, Alcon Pharmaceuticals, Alimera Sciences, Inc., Alkermes, Allergan, ANI Pharmaceuticals, Amgen, Annexon, Apellis Pharmaceuticals, Inc., Astellas; Bausch and Lomb, Bayer Healthcare Pharmaceuticals, Inc., Biocryst, Ceryvyn, Coherus, EyePoint Pharmaceuticals, Genentech, Harrow, Novartis, Ocular Therapeutix, Oculis, Optos, Inc., Outlook Therapeutics, Oxular, Regeneron, REGENXBIO, RetinaAI, Roche, Sanofi, Santen, Inc.
- **Research Support:** 4DMT, Adverum, Annexon Biosciences, Ceryvyn Therapeutics, Eyebio, Eyepoint Pharma, Genentech, Kodiak Sciences, Ocular Therapeutix, Inc, Oculis, Regeneron, RegenxBio, Sanofi.
- **Speaker:** Amgen, ANI Pharmaceuticals, Apellis, Genentech, Regeneron

Arshad M. Khanani

- **Consultant:** Abbvie, ADARx Pharmaceuticals, Adverum, Alcon, Alkermes, Allgenesis, Amgen, Annexin, Annexon, Apellis Pharmaceuticals, Ashvattha, Therapeutics, Astellas, Aviceda Therapeutics, Beacon Therapeutics, Boehringer Ingelheim, Clearside Biomedical, Complement Therapeutics, Ceryvyn Therapeutics, 4DMT, Entarada, Exegenesis, EyePoint Pharmaceuticals, Fronterra Therapeutics, Genentech, Harrow, i-Lumen Scientific, InFocus, Janssen Pharmaceuticals, Kriya Therapeutics, Kyowa Kirin, Lexitas, Merit, Neurotech, Nanoscope, Novartis, Ocugen, Ocular Therapeutix, Oculis, Ollin, Opus Genetics, Perfuse, Recens Medical, Regeneron Pharmaceuticals, Regenxbio, Revive, RevOpsis, Roche, Samsung, Sanofi, Stealth BioTherapeutics, Sun Pharma, Surrozen, Thea Pharma, Therini, Unity Biotechnology, Vanotech, Vial, ZipBio
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- **Board of Directors:** Oculis

Agenda

- **The Unmet Need**
Mark R. Barakat, MD, FASRS
- **Science Behind OTX-TKI**
Dilsher S. Dhoot, MD, FASRS
- **SOL-1 Trial Design and Results**
Arshad M. Khanani, MD, MA, FASRS

- **SOL-1 Clinical Evidence**
Mark Barakat, MD, FASRS
- **Discussion**
Moderator: Arshad M. Khanani, MD, MA, FASRS

The Unmet Need

Mark R. Barakat, MD, FASRS

Treatment Burden Remains a Significant Unmet Need in nAMD

INJECTION BURDEN

up to
12 anti-VEGF injections/yr for patients¹



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 activities³

40% discontinue treatment in the first year due to heavy treatment burden⁴

Suboptimal Frequency of Injections Contribute to Declining Real-World Outcomes

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Review Article

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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}

^aInstitut de la Màcula and Barcelona Macula Foundation, Barcelona, Spain; ^bCenter for Ophthalmic Bioinformatics, Cole Eye Institute, Cleveland Clinic, Cleveland, OH, USA; ^cDepartment of Ophthalmology, University Vita-Salute, Scientific Institute San Raffaele, Milan, Italy; ^dDepartment of Ophthalmology, Hôpital Intercommunal de Creteil, Creteil, France; ^eNovartis Pharma AG, Basel, Switzerland; ^fDepartment of Ophthalmology, York Teaching Hospitals NHS Foundation Trust and Department of Health Sciences, University of York, York, UK; ^gYork Teaching Hospitals, York, UK

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 in-

jections and monitoring visits imposed on patients/caregivers. However, another primary reason is the general mindset in the ophthalmological community that sustained benefits with treatment are not possible, leading to poor compliance and creating a vicious circle. **Conclusions:** Initial VA gains can be maintained with more intensive/proactive approaches. Promising new treatments requiring less frequent injections/monitoring will help in the near future; meanwhile, better results could be achieved by changing the community mindset that contributes to undertreatment.

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Introduction

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



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. Wyckoff, MD, PhD,¹ Vincent Garmo, MHS,² David Tabano, PhD,² Alicia Menezes, MD,² Eunice Kim, RPh, MS,² Helene B. Fevrier, MS,² Andrew LaPrise, BS,² Theodore Leng, MD, MS²

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.

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Supplemental material available at www.ophtalmologyscience.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.^{14–19} To maintain the benefits of anti-VEGF, most patients must continue to receive regular

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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^{1,5}

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-naïve nAMD patients who underwent anti-VEGF injections between January 1, 2012, and October 31, 2016, were eligible if follow-up data were available before October 31, 2017.

Methods: Age, gender, anti-VEGF treatment type, number of treatments, and VA were extracted from the database.

Main Outcome Measure: Mean VA change assessed at 1 year and stratified based on number of anti-VEGF injections received over 1 year.

Results: In this analysis, 49 485 eyes were included. The mean age was 80.9 years, and 64% were female. Mean baseline VA was 53.8 letters (Snellen equivalent, 20/80). At 1 year, after a mean of 7.3 anti-VEGF injections, there was a mean gain of 1 letter (0.95 letter; 95% confidence interval [CI] for change in VA, +0.77 to +1.13 letter; $P < 0.001$). When stratified by anti-VEGF agent, the mean VA changes were nearly identical at 1 year. There was a linear relationship between mean letters gained and mean number of injections, between 4 and 10 injections over 1 year, with 4 or fewer or 10 or more injections associated with loss of vision or a plateau, respectively. Greater mean 1-year change in VA also trended with worse baseline VA; those patients with better VA at presentation tended to be particularly vulnerable to vision loss. Those who received the fewest injections tended to be older and have worse baseline VA.

Conclusions: Real-world nAMD patients receive fewer anti-VEGF injections and experience worse visual outcomes compared with patients receiving fixed, frequent therapy in randomized controlled trials. Mean change in VA correlates with treatment intensity at 1 year, but with ceiling effects related to treatment intensity and baseline VA. Older patients and those with poor baseline VA may be particularly prone to undertreatment. *Ophthalmology Retina* 2020;4:19–30 © 2019 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

See Editorial on page 1.

Anti-vascular endothelial growth factor (VEGF) therapy currently is the standard of care for neovascular age-related macular degeneration (nAMD). Registration trials for ranibizumab (monthly) and aflibercept (every 2 months after 3 monthly loading doses), as well as the monthly ranibizumab and bevacizumab arms of the Comparison of Age-Related Macular Degeneration Treatments Trials (CATT); described further in Table 1), suggest that these anti-VEGF agents can perform similarly, with an average 1-year improvement of 8.5

letters across these studies (Table 1).^{1–4} However, real-world studies of anti-VEGF therapy in nAMD, based on chart reviews, electronic medical records (EMRs), or claims analyses, have reported less favorable visual outcomes.^{5–19} For example, our prior study showed no improvement in visual acuity (VA) in the 1-year cohort,¹⁸ and another United States–based real-world study reported a 1-year improvement of only 2.5 letters, with both studies excluding nAMD patients receiving fewer than 3 anti-VEGF injections.¹⁹

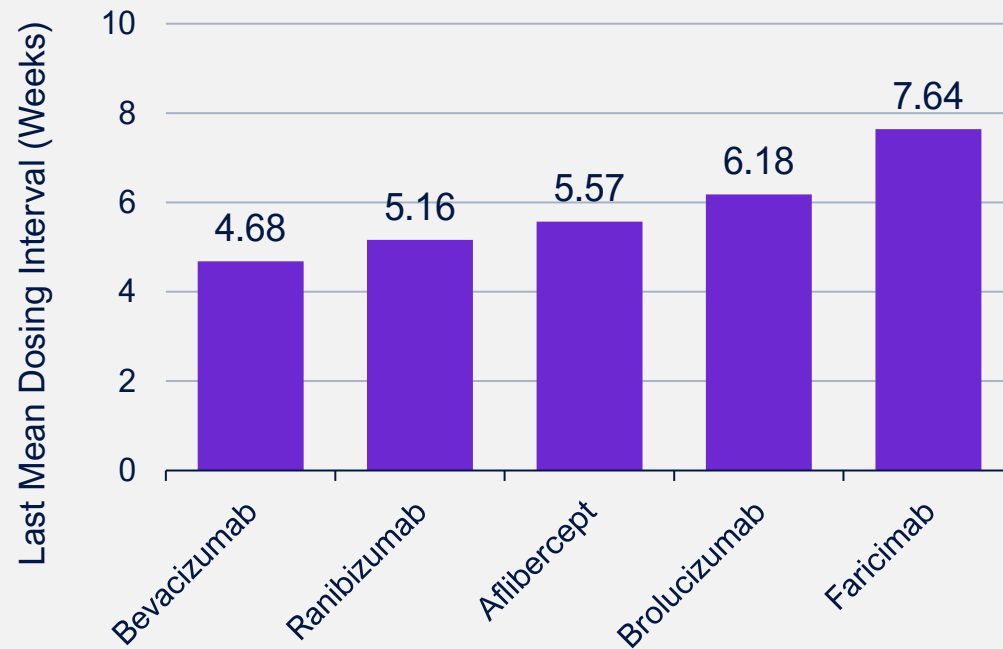
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Second Generation nAMD Agents Extend Injection Intervals Incrementally Over Previous Agents in the Real World

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

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

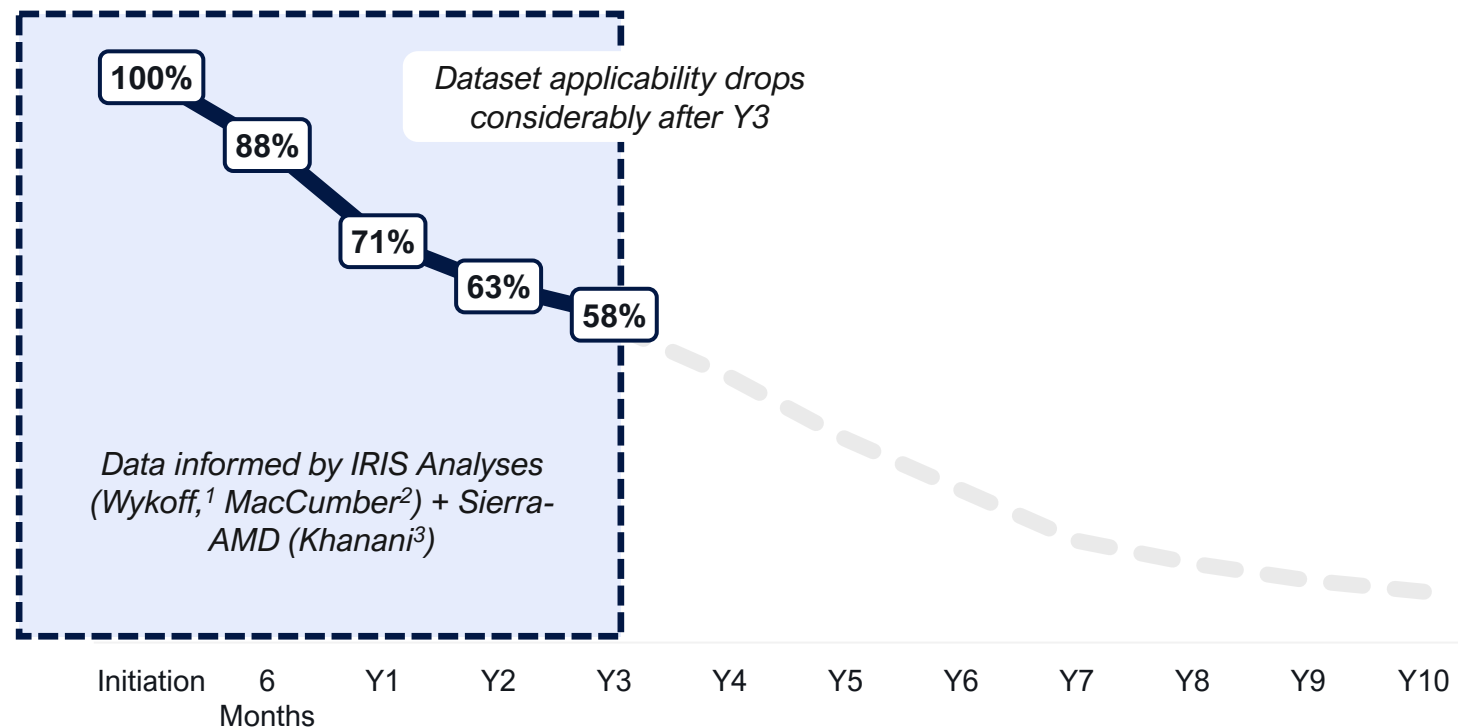
Limited Longer-Term Follow-Up

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

Attrition appeared to be a secondary focus

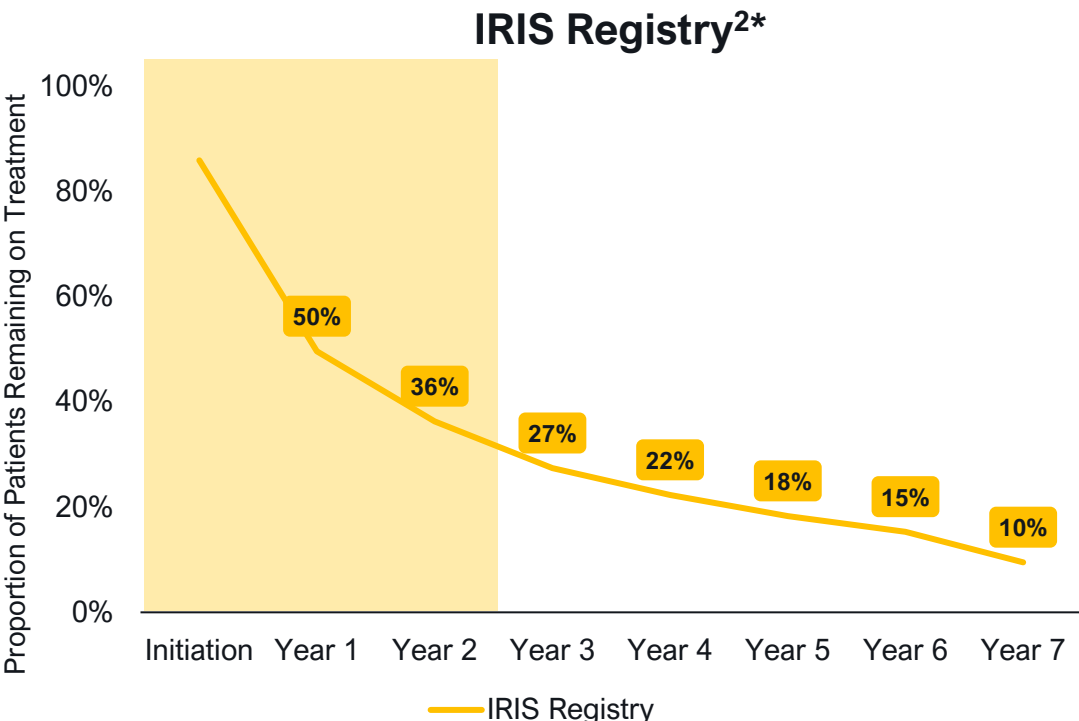
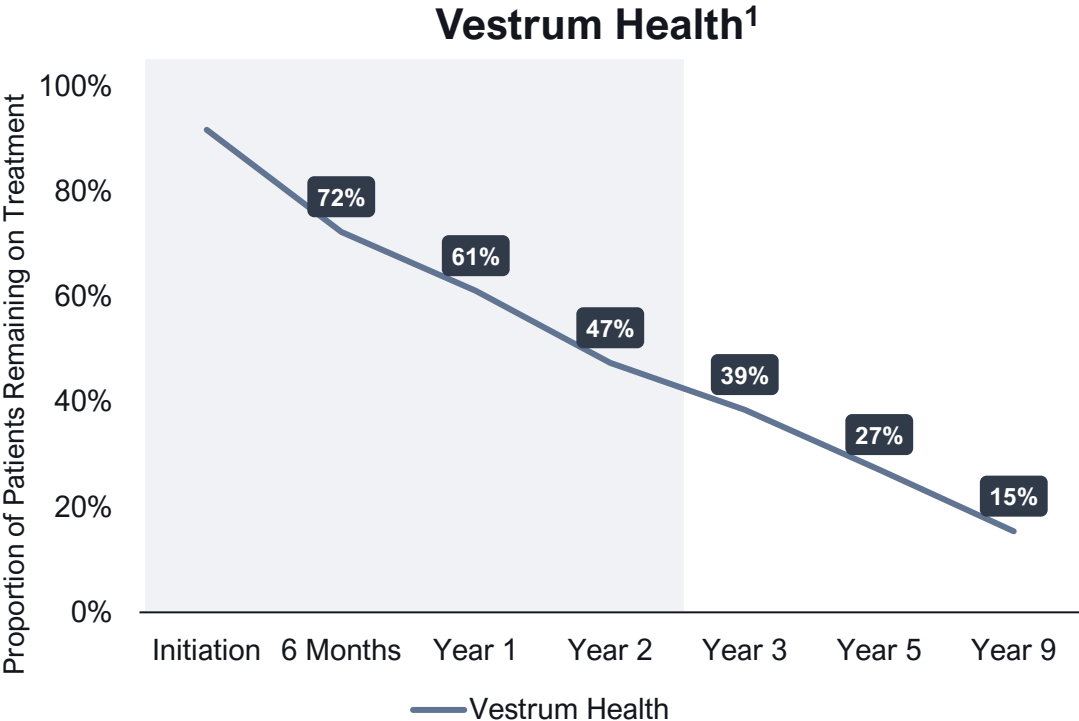
in large registry analyses with anti-VEGFs in nAMD

Literature-Based Attrition Curve*



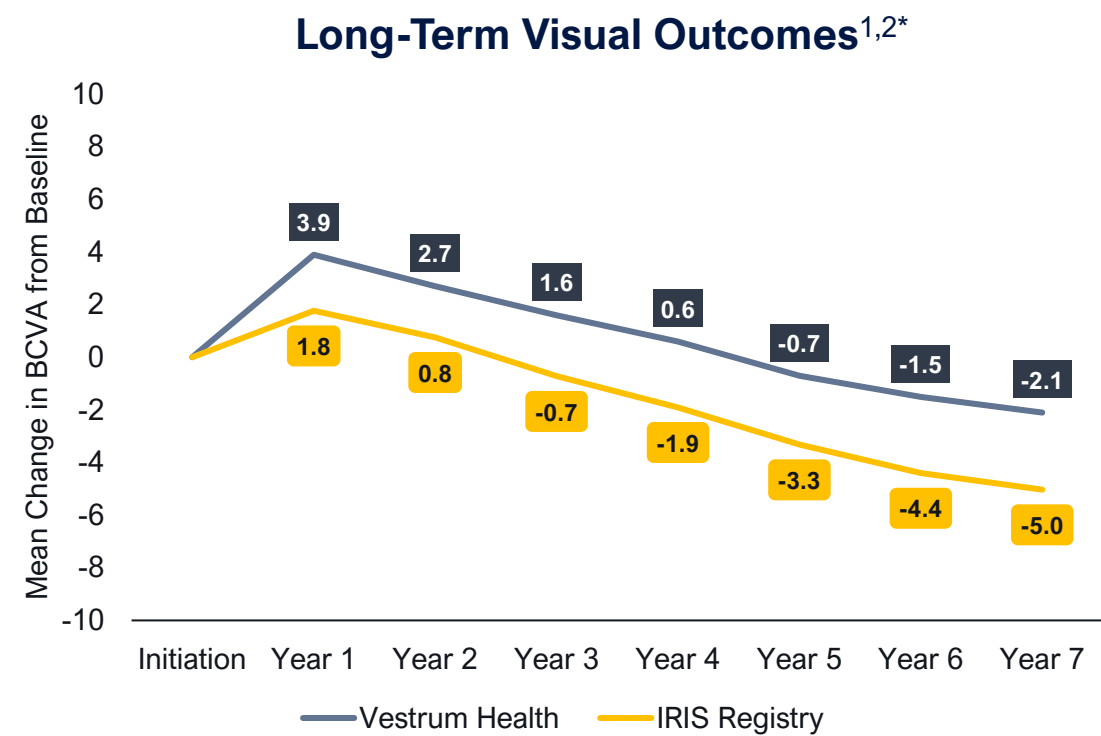
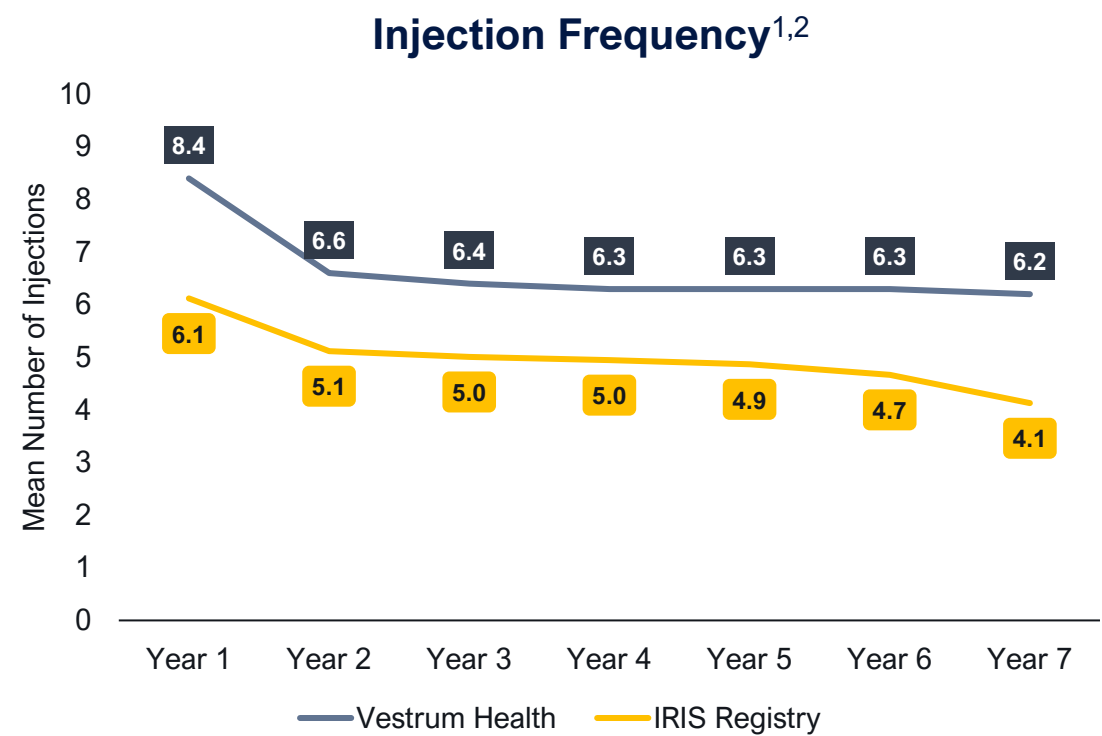
High Real-World Discontinuation Highlights Unmet Need for Durable, Low-Burden nAMD Therapy

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



*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 Therapeutics. 2026. 2. Data on File 047. Ocular Therapeutics. 2026.
IRIS, Intelligent Research in Sight

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



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

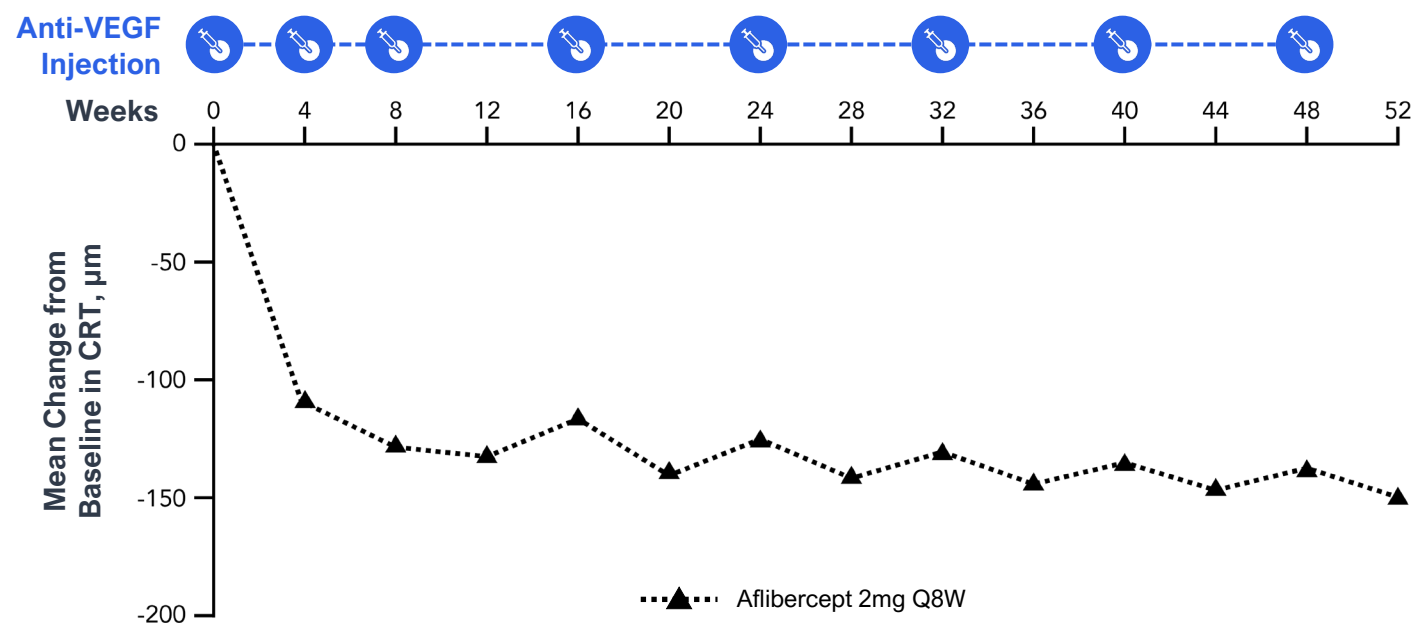
Greater Retinal Thickness Variability During Anti-VEGF Therapy is Associated with Suboptimal Anatomic and Visual Outcomes

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



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

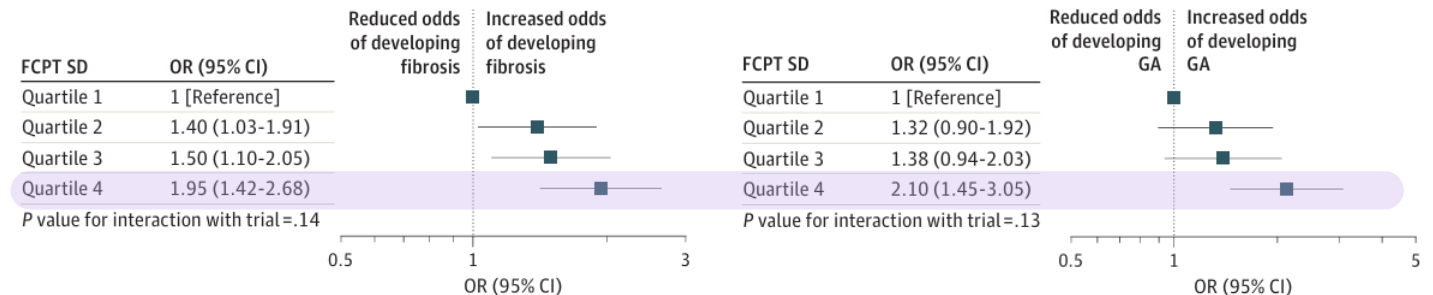
Retinal Thickness
Fluctuations

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

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

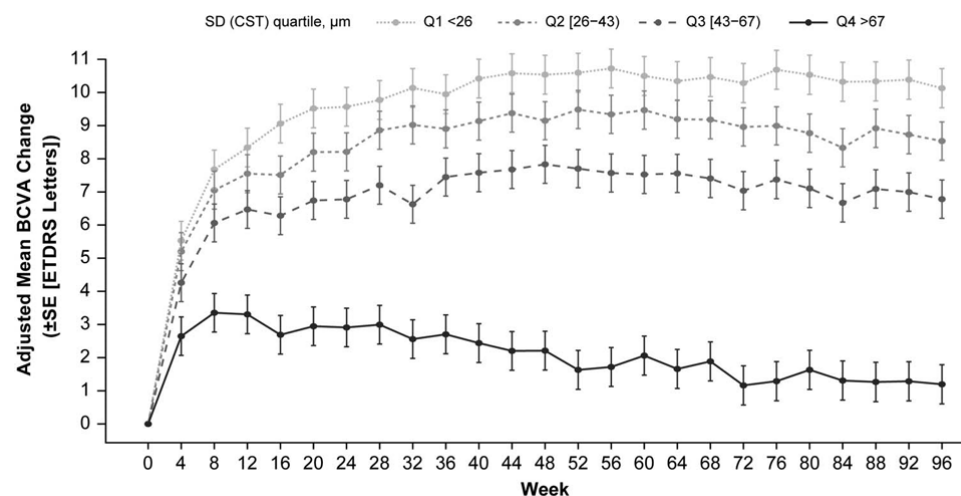
Retinal Thickness
Fluctuations

Development of
Fibrosis and Atrophy

Poorer Long-Term
Visual Outcomes

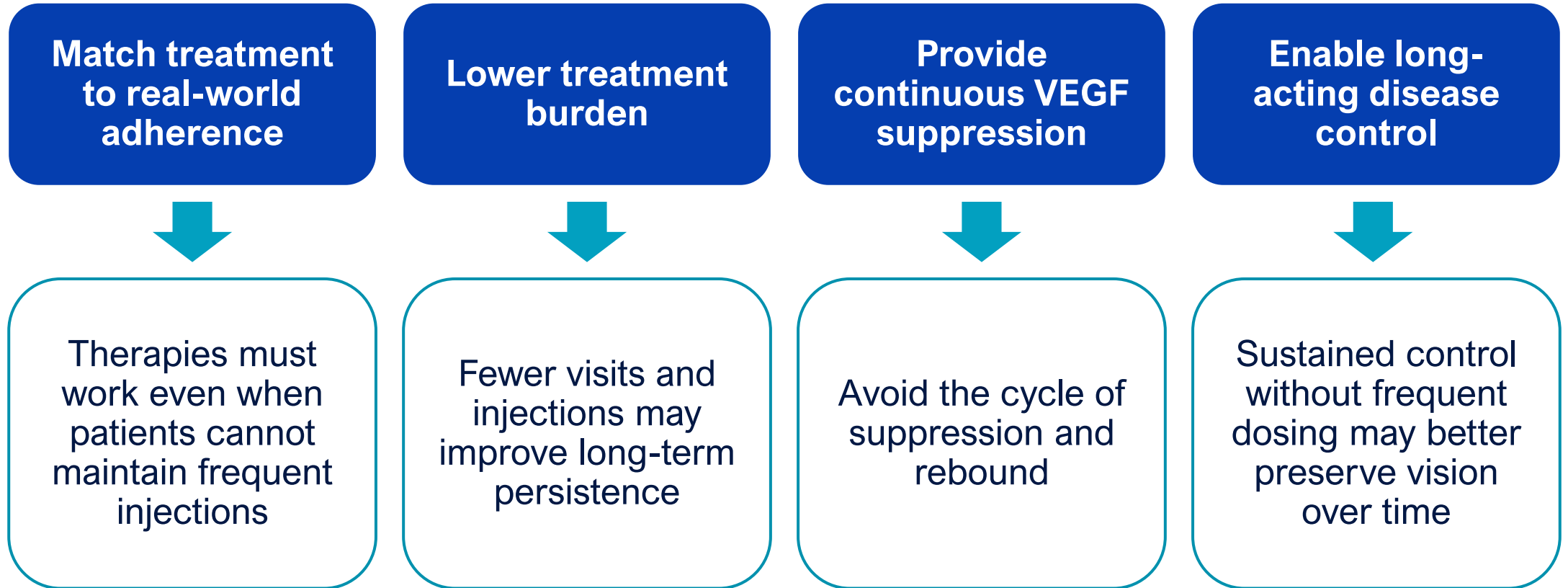
EFFECT OF RETINAL THICKNESS VARIABILITY ON VISUAL OUTCOMES AND FLUID PERSISTENCE IN NEOVASCULAR AGE-RELATED MACULAR DEGENERATION

A Post Hoc Analysis of the HAWK and HARRIER Studies



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

Redefining nAMD Therapy: What can we do better?

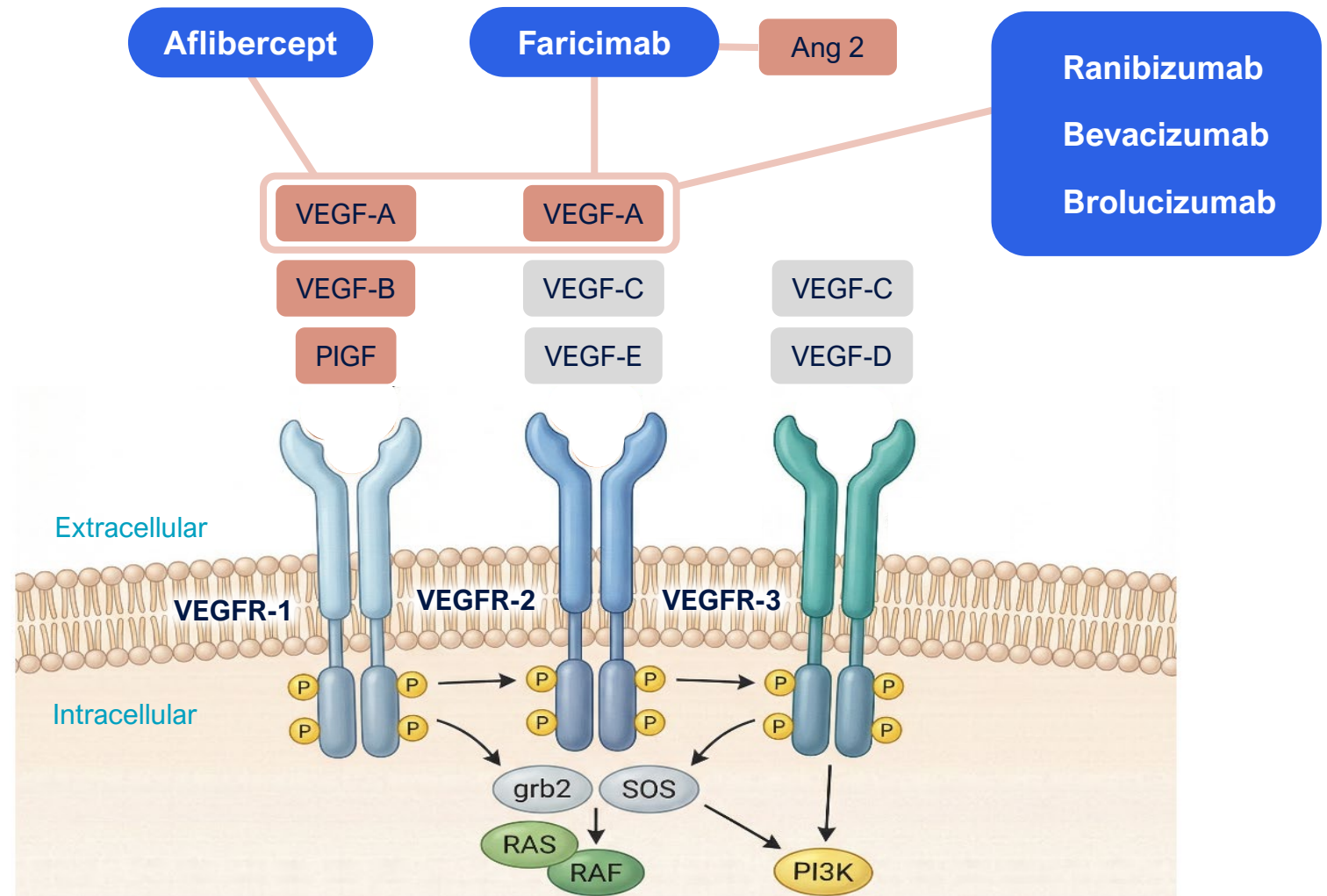


Science Behind OTX-TKI

Dilsher S. Dhoot, MD, FASRS

Current Anti-VEGF Therapies Selectively Target Only Extracellular VEGF

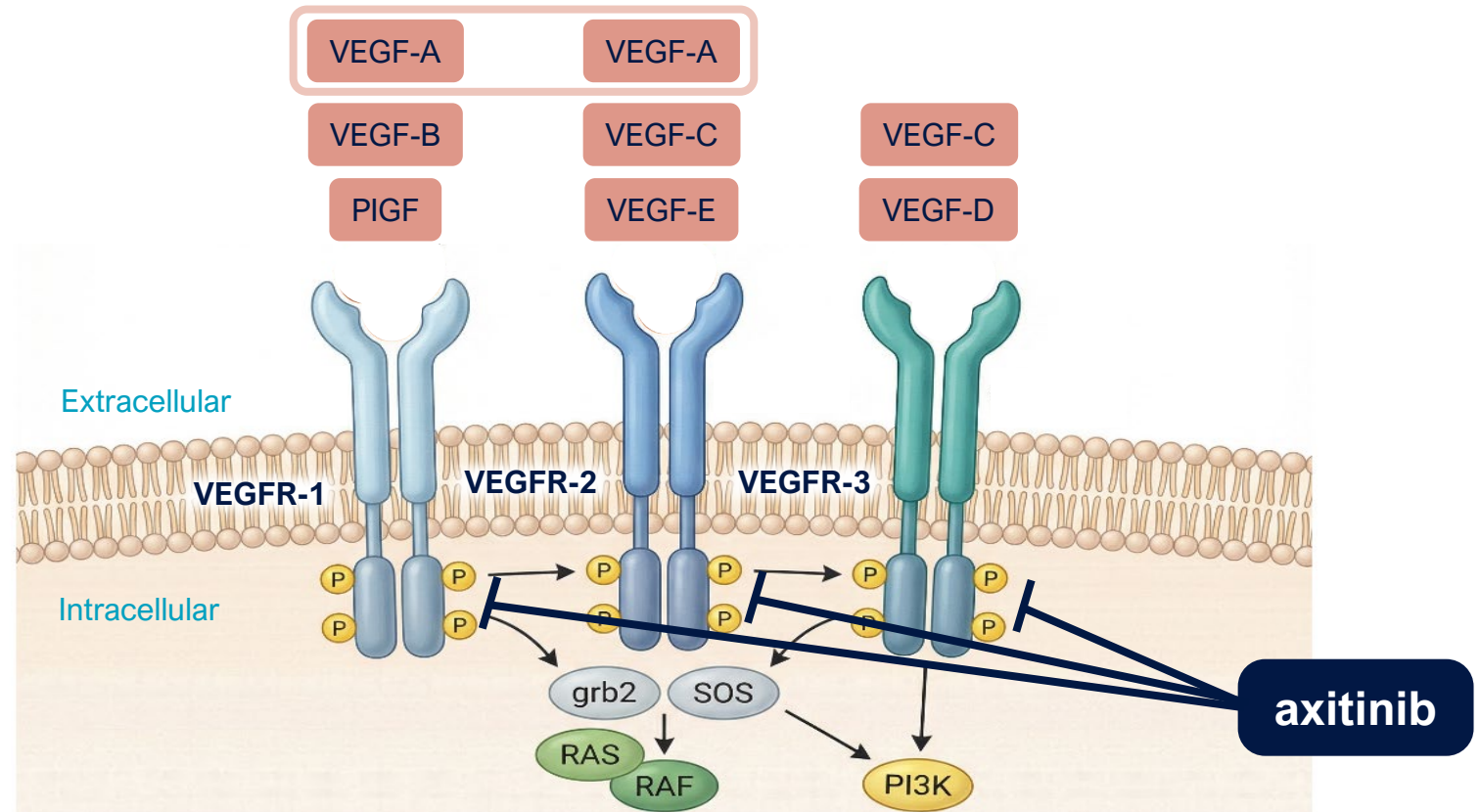
Current **Anti-VEGF** agents act **extracellularly by binding selective ligands**, like VEGF-A, preventing receptor binding and activation^{1,2}



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

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}

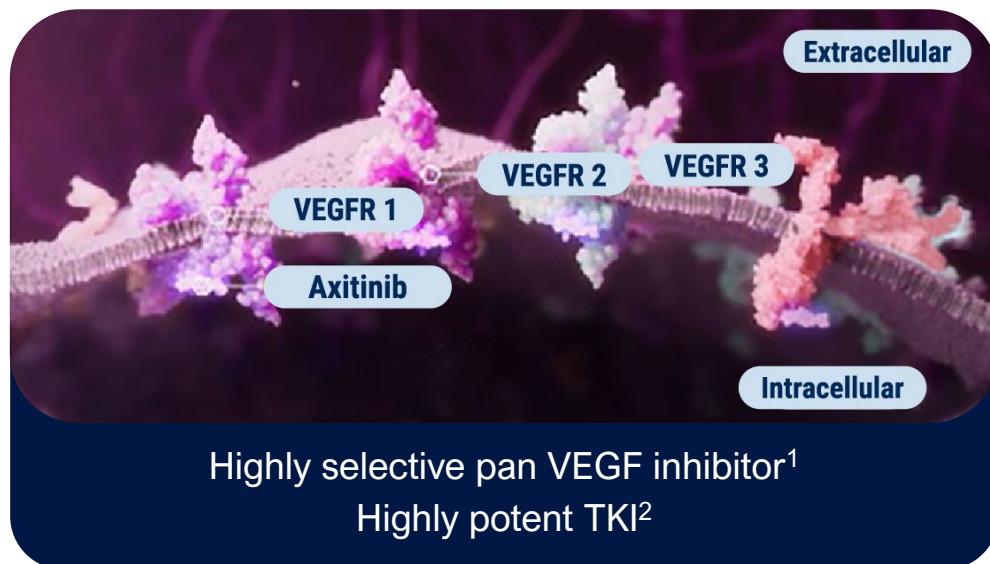


Select angiogenesis intracellular targets of inhibition for tyrosine kinase inhibitors. Adapted from Zhao et al. 2015.²⁻⁴

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

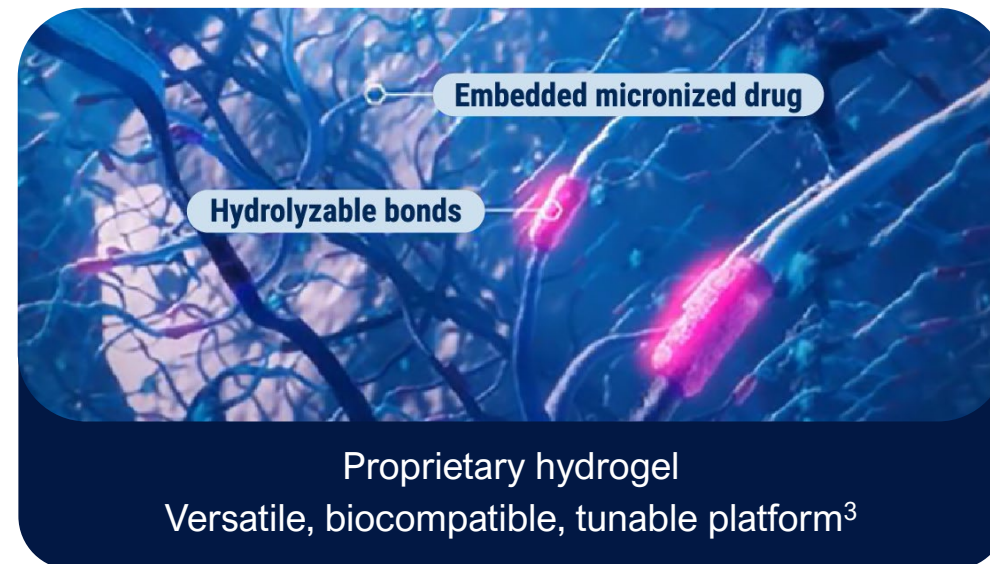
AXITINIB

Multi-target Tyrosine Kinase Inhibitor (TKI)



HYDROGEL TECHNOLOGY

Bioresorbable, Sustained Drug Delivery



+

OTX-TKI

is being developed with the aim to provide:

A single hydrogel insert^{3,4}

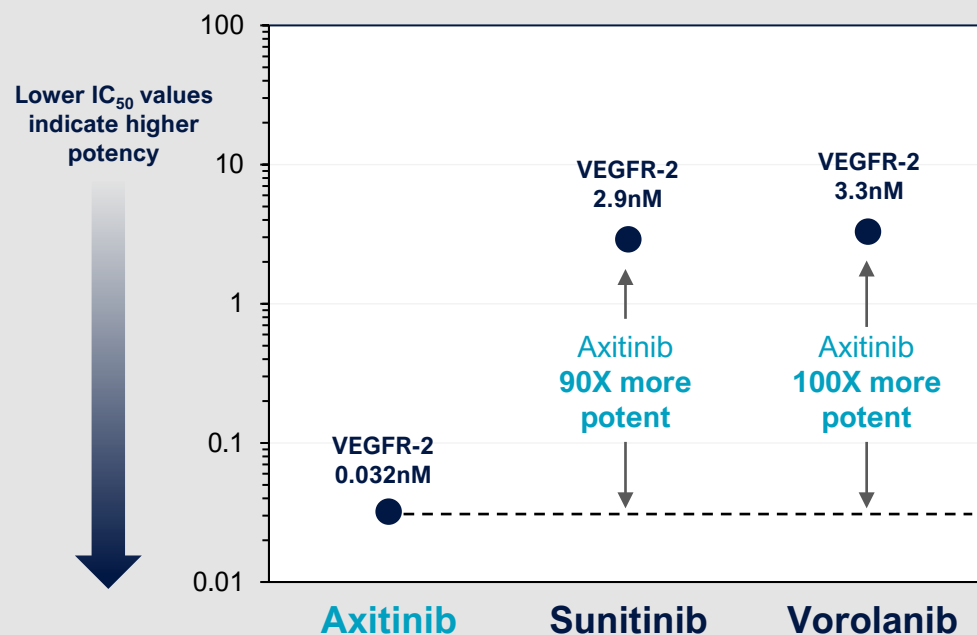
Continuous and consistent
delivery up to 12 months^{3,5}

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.

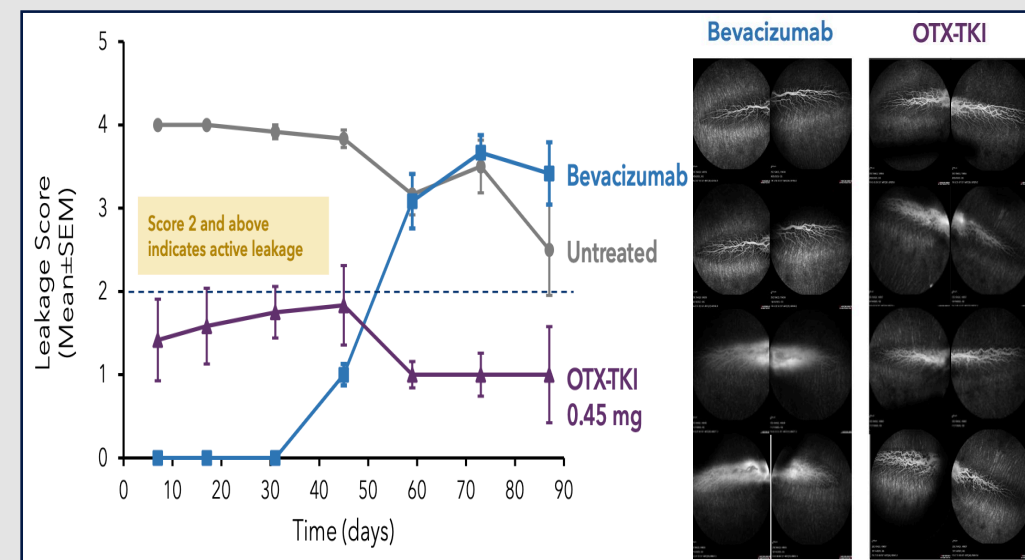
Axitinib: Highly Selective, Very Potent, pan-VEGFR Inhibitor

IC₅₀ for VEGF Receptor 2 (nM)¹⁻³



Highly selective for all VEGF receptors, ~100x more potent for VEGFR-2¹⁻³

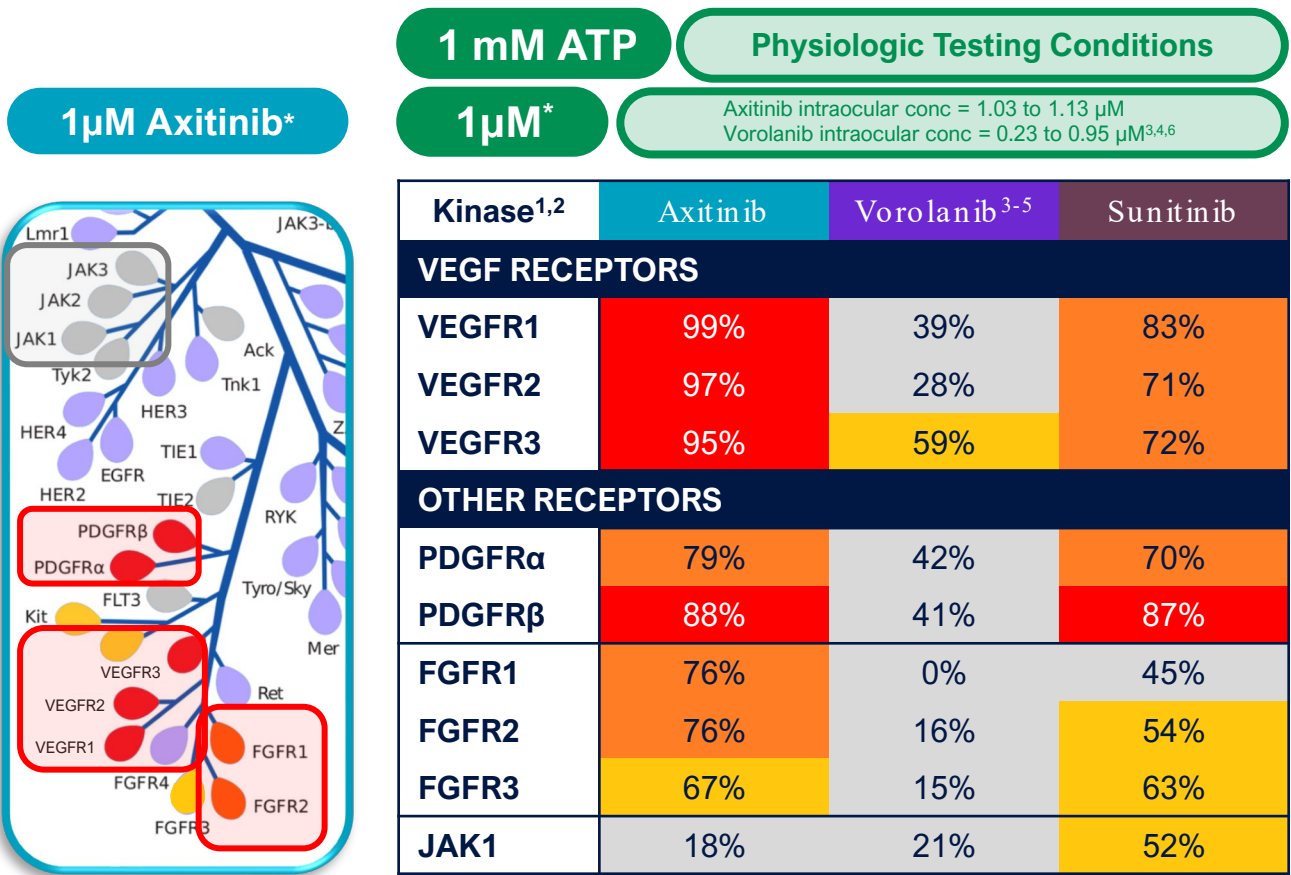
VEGF Challenge Rabbit Model²



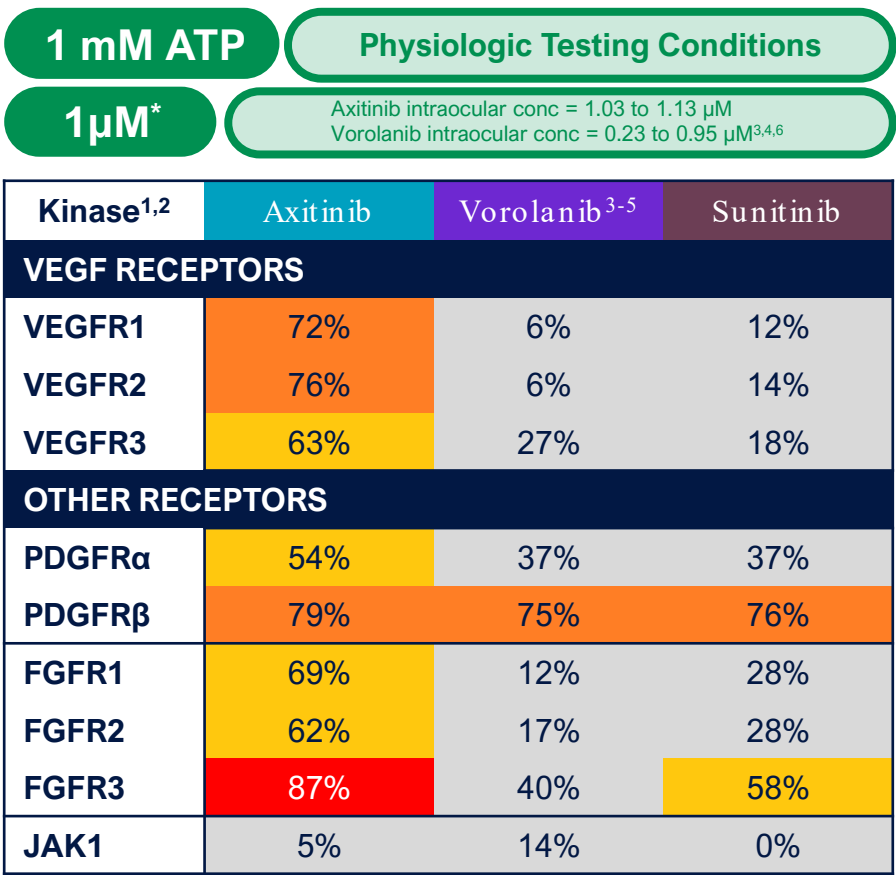
Sustained leakage control in repeat VEGF challenge animal model²

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

AssayQuant (Fluorescence Assay)*

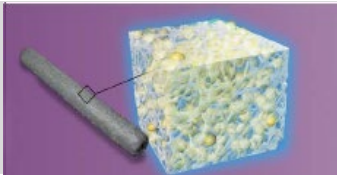
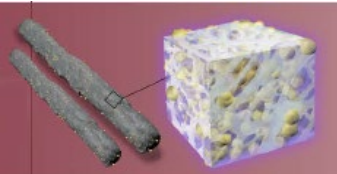
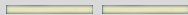
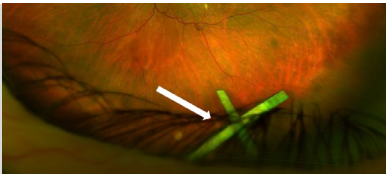
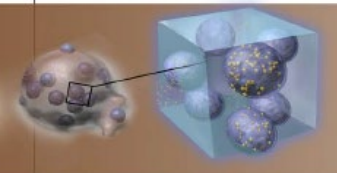
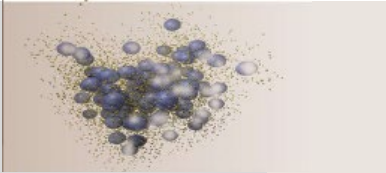
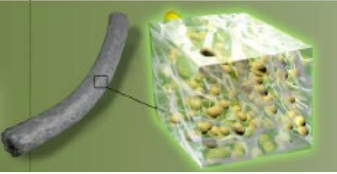


Reaction Biology (Radiometric Assay)**



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

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 VIBRANT VISION		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. Images of EYP-1901 implants from Abbey, AM. Topline Data from DAVIO 2: a Phase 2 Study of a Single Injection of DURAVYU (Vorolanib Intravitreal Insert). Presented at Retina World Congress. Fort Lauderdale, FL; May 9-12, 2024.

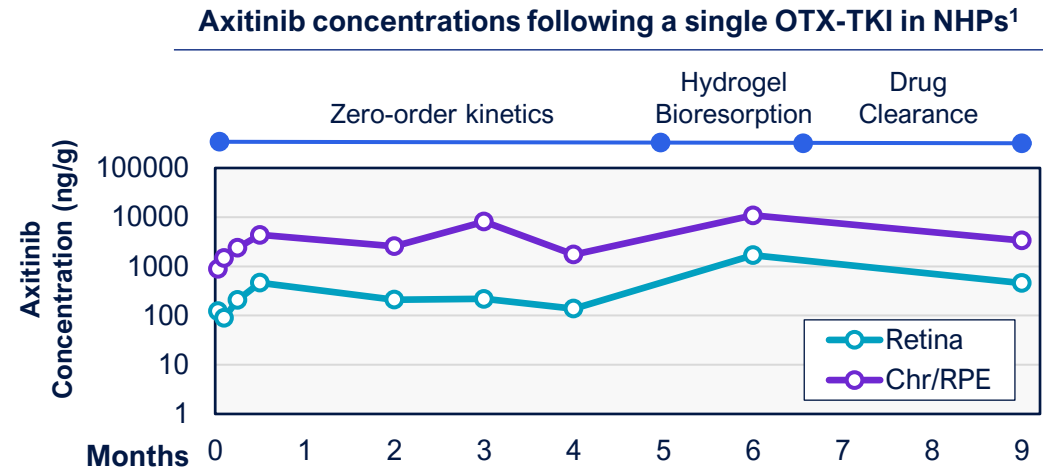
*. Li M, et al. *Heliyon*. 2022;8(12):e12219. †. Pellegrini GABP, et al. *Int J Retina Vitreous*. 2025;11(1):7. ‡. Kim JT, et al. *Retina*. 2020; 40(11):p 2226-2231. §. Schmit-Eilenberger VK. *Clin Ophthalmol*. 2015;9:801-811. ¶. Diameter of EYP-1901 unconfirmed; EyePoint Pharmaceuticals. Clinical Study 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

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

OTX-TKI In Vivo Delivery Profile¹

Rapid, continuous and consistent axitinib delivery

Targeted drug delivery to retina and choroid



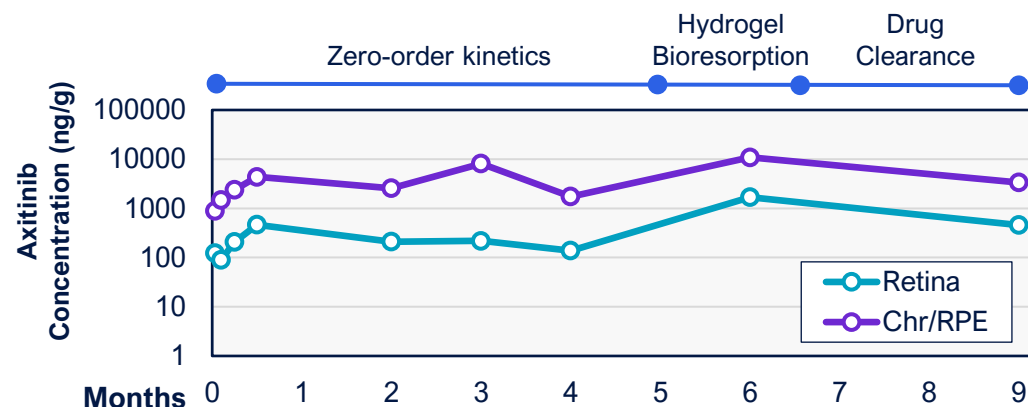
OTX-TKI is Designed to Release Axitinib and Maintain Intraocular Drug Levels Over Time with Complete Bioresorption

OTX-TKI In Vivo Delivery Profile¹

Rapid, continuous and consistent axitinib delivery

Targeted drug delivery to retina and choroid

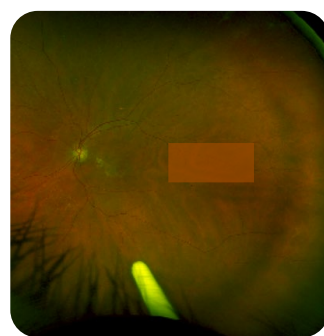
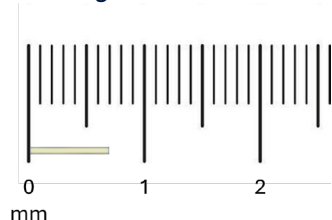
Axitinib concentrations following a single OTX-TKI in NHPs¹



Hydrogel bioresorbs completely and predictably via hydrolysis for potential redosing¹⁻³

Dry OTX-TKI Dimensions

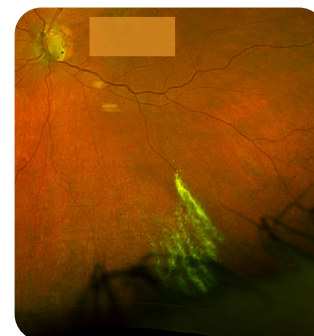
7mm length, 0.4mm diameter



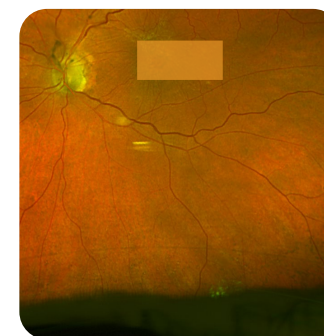
Day 1



Week 20



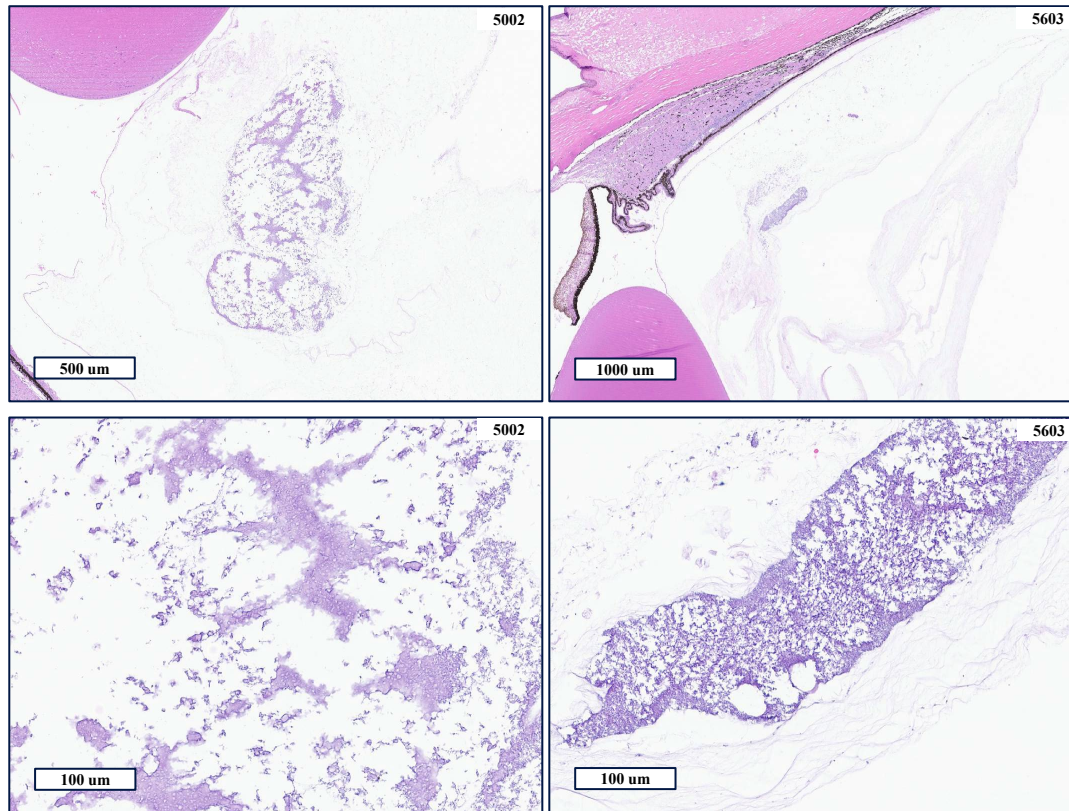
Week 32



Week 44

Histology of Ocular Tissues Demonstrates Axitinib Elution with No Inflammatory Cells

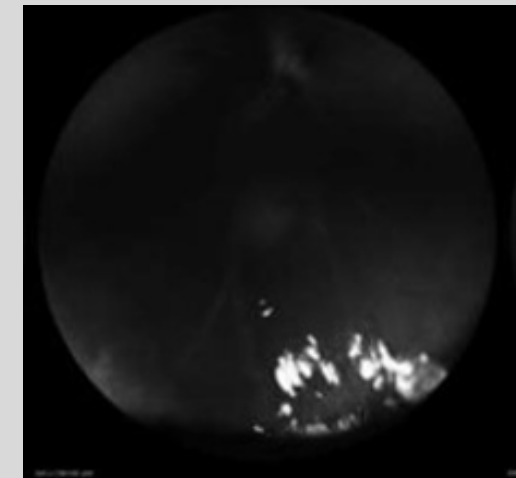
Histology of Ocular Tissues from 0.7 mg OTX-TKI in NHPs



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

OTX-TKI is Designed for Seamless, Immediate Adoption

Ideal Target Product Profile

Pan-VEGF and PDGF
inhibitory activity¹

Axitinib has best-in-class
(TKI) potency¹

Extended durability
up to 12 months²

Single Bioresorbable Hydrogel

No remnants³

Tunable hydrogel⁴

Hydrogel used
in over 5 million patients⁵

Optimizing for Retina Practices

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

Predictable
schedule for patients²

Designed for **improved**
treatment adherence²

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

OTX-TKI Phase 3 Clinical Programs

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

wet AMD

REGISTRATIONAL TRIAL

SOL-1

Superiority Trial

Durability of a single
OTX-TKI injection

REGISTRATIONAL TRIAL

SOL-R

Non-Inferiority Trial

Repeat dosing
every 6 months

EXTENSION STUDY

SOL-X

Open-Label Extension

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

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

NPDR

REGISTRATIONAL TRIAL

HELIOS-3

Superiority Trial

12-month dosing
intervals with repeat
dosing

OTX-TKI Phase 3 Clinical Programs

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

wet AMD

REGISTRATIONAL TRIAL

SOL-1

Superiority Trial

Durability of a single
OTX-TKI injection

REGISTRATIONAL TRIAL

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Repeat dosing
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EXTENSION STUDY

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Long-term safety and
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NPDR

REGISTRATIONAL TRIAL

HELIOS-3

Superiority Trial

12-month dosing
intervals with repeat
dosing

SOL-1: Trial Design and Results

Arshad M. Khanani, MD, MA, FASRS

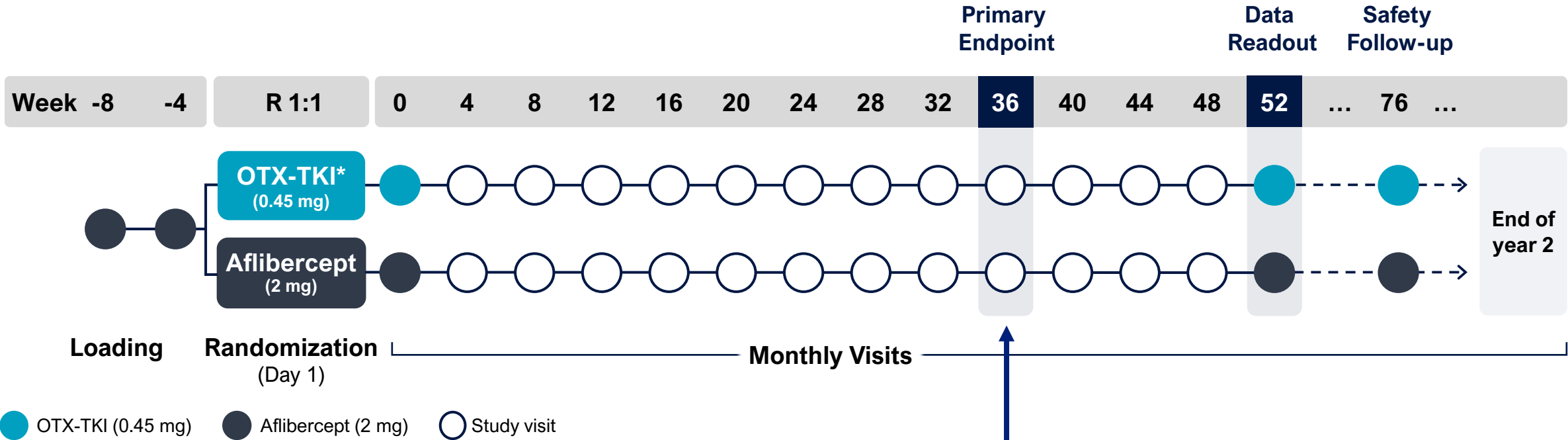
OTX-TKI Evaluated in a Superiority nAMD Trial Designed to Align with FDA Guidance

	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	Decrease  ≥15-Letter ¹ Increase  Difference	✓	≥15-Letter Decrease Proportion with <15 ETDRS letters of BCVA loss from baseline at Week 36



- 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**

Study Design: OTX-TKI and Aflibercept Direct Comparison

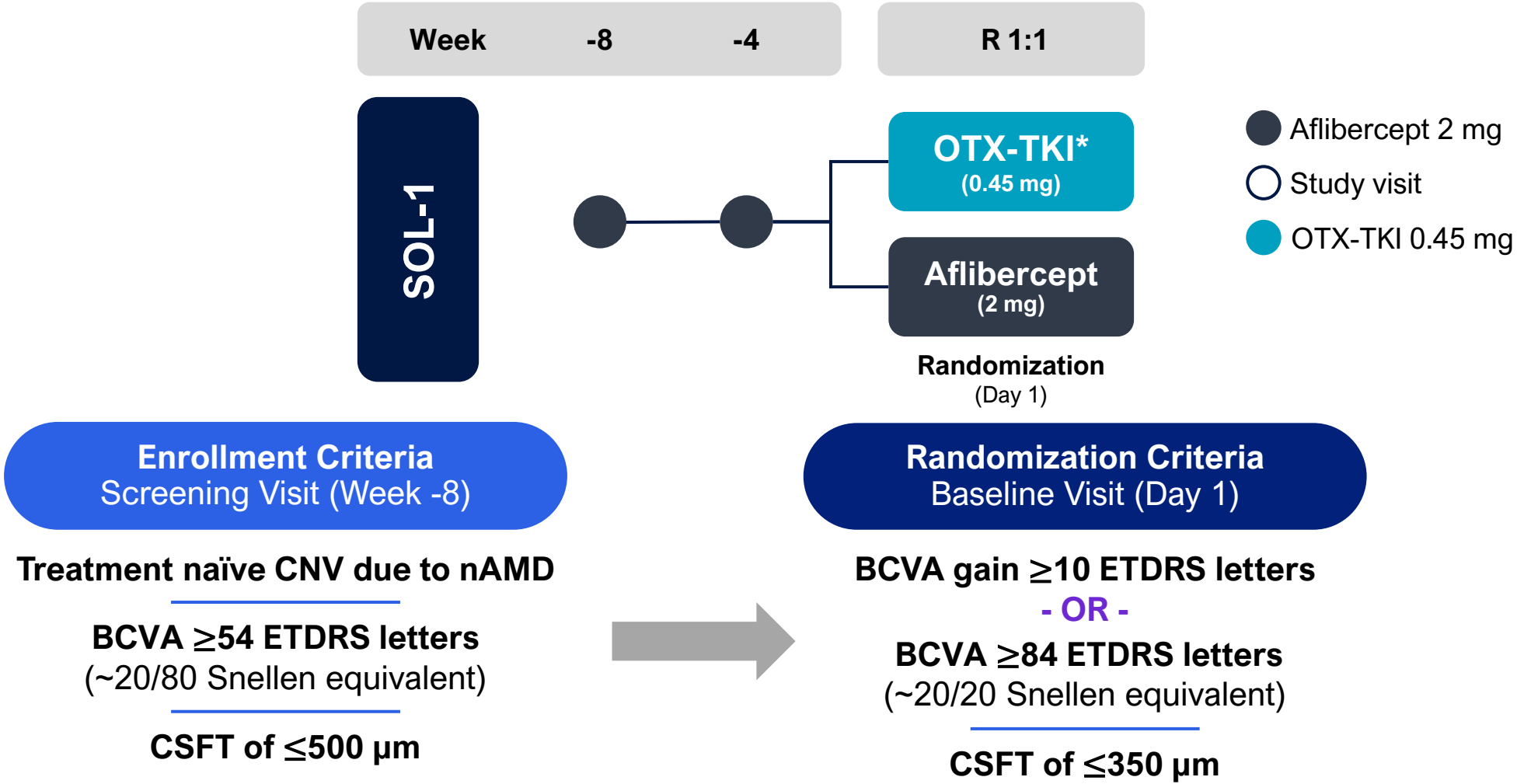


Rescue Treatment Criteria
BCVA loss ≥ 15 ETDRS letters from baseline due to nAMD
— OR —
New macular hemorrhage that would likely lead to irreversible vision loss if left untreated in the opinion of the investigator after discussion with Medical Monitor

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

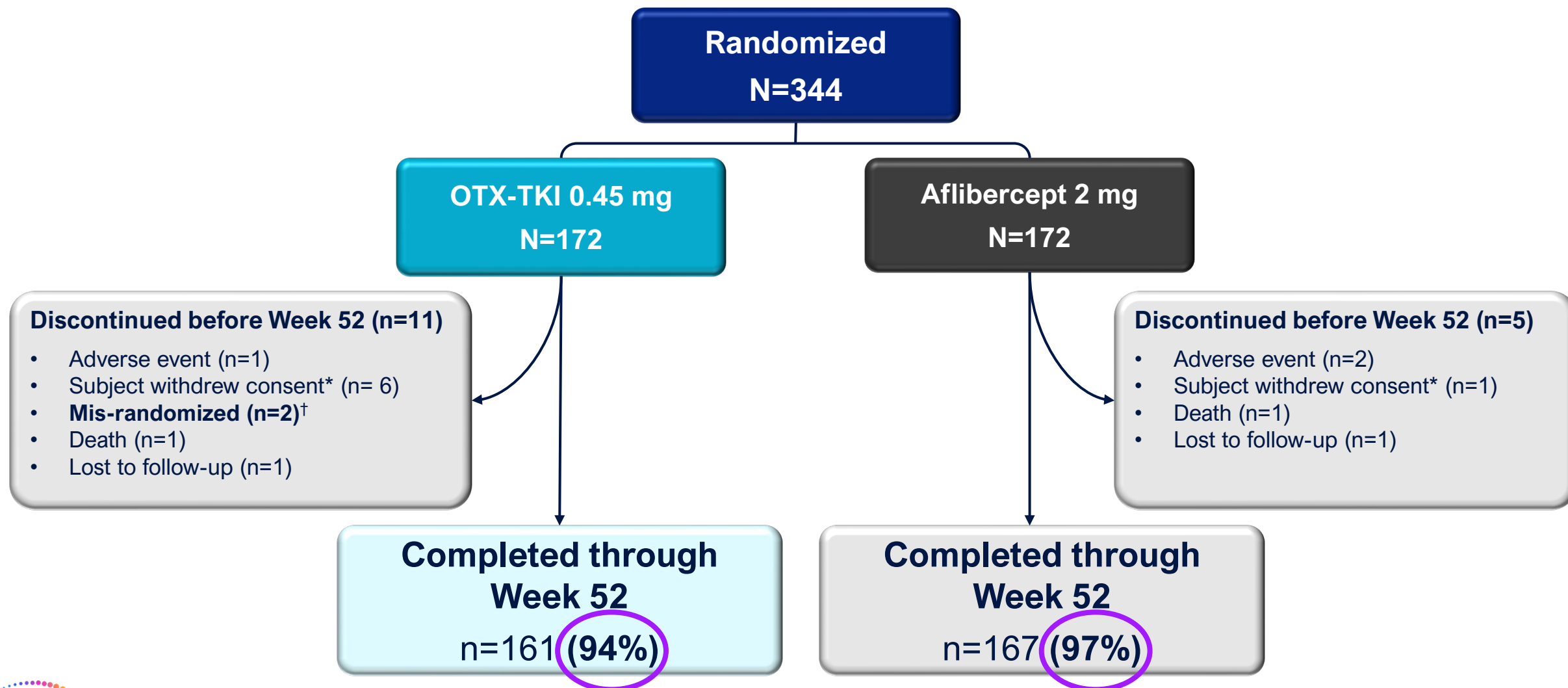
Eligibility and Enrollment Criteria

Key Inclusion Criteria



Strong Subject Retention Maintained through Week 52

Subject Disposition



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	107 (62.9)	114 (67.1)
≥ 84 ETDRS letters (~20/20)	63 (37.1)	56 (32.9)

Anatomic Improvement Observed After Two Aflibercept Injections

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)

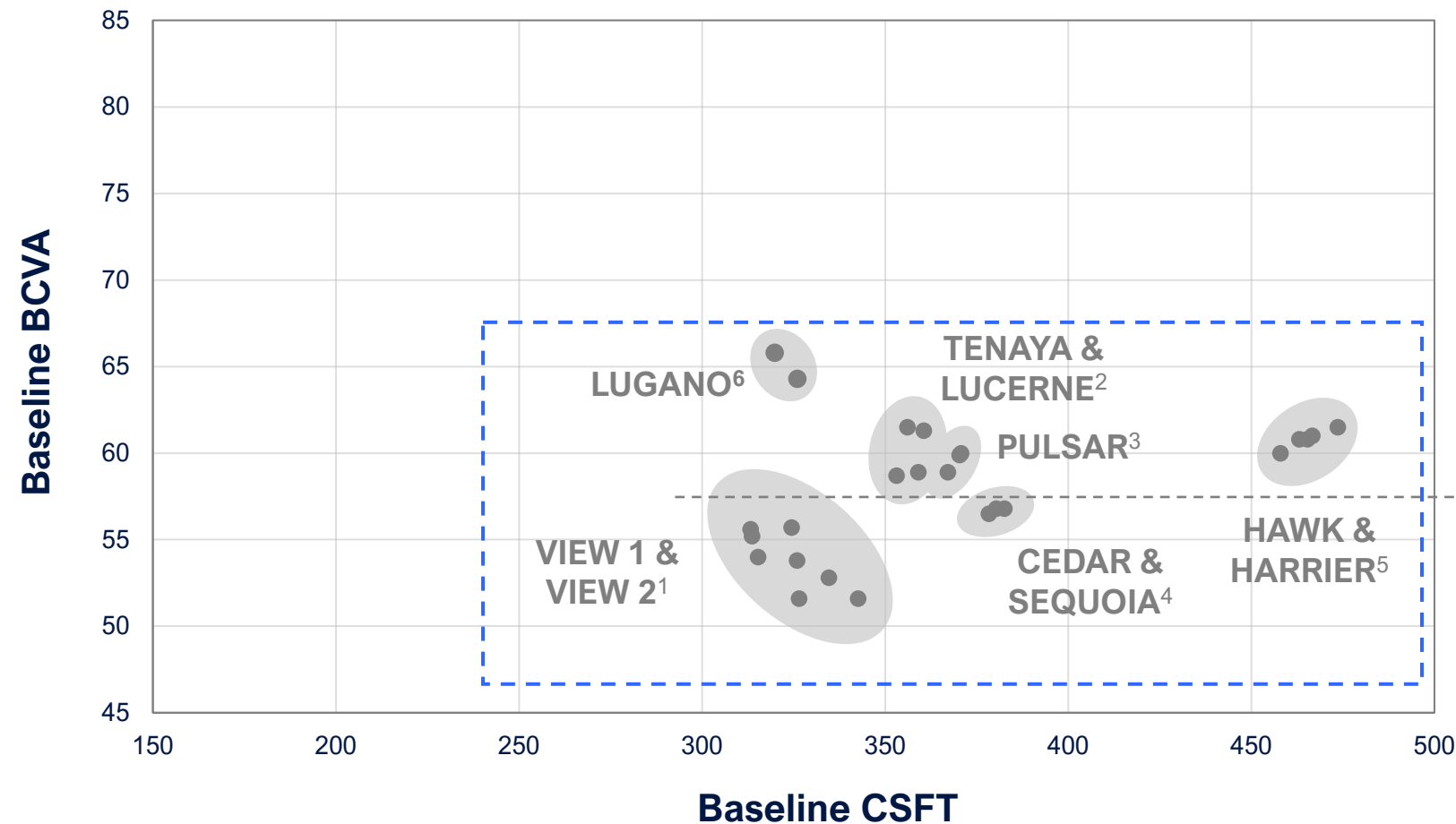
Baseline (Randomization)

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)

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



Baseline BCVA Across nAMD Trials

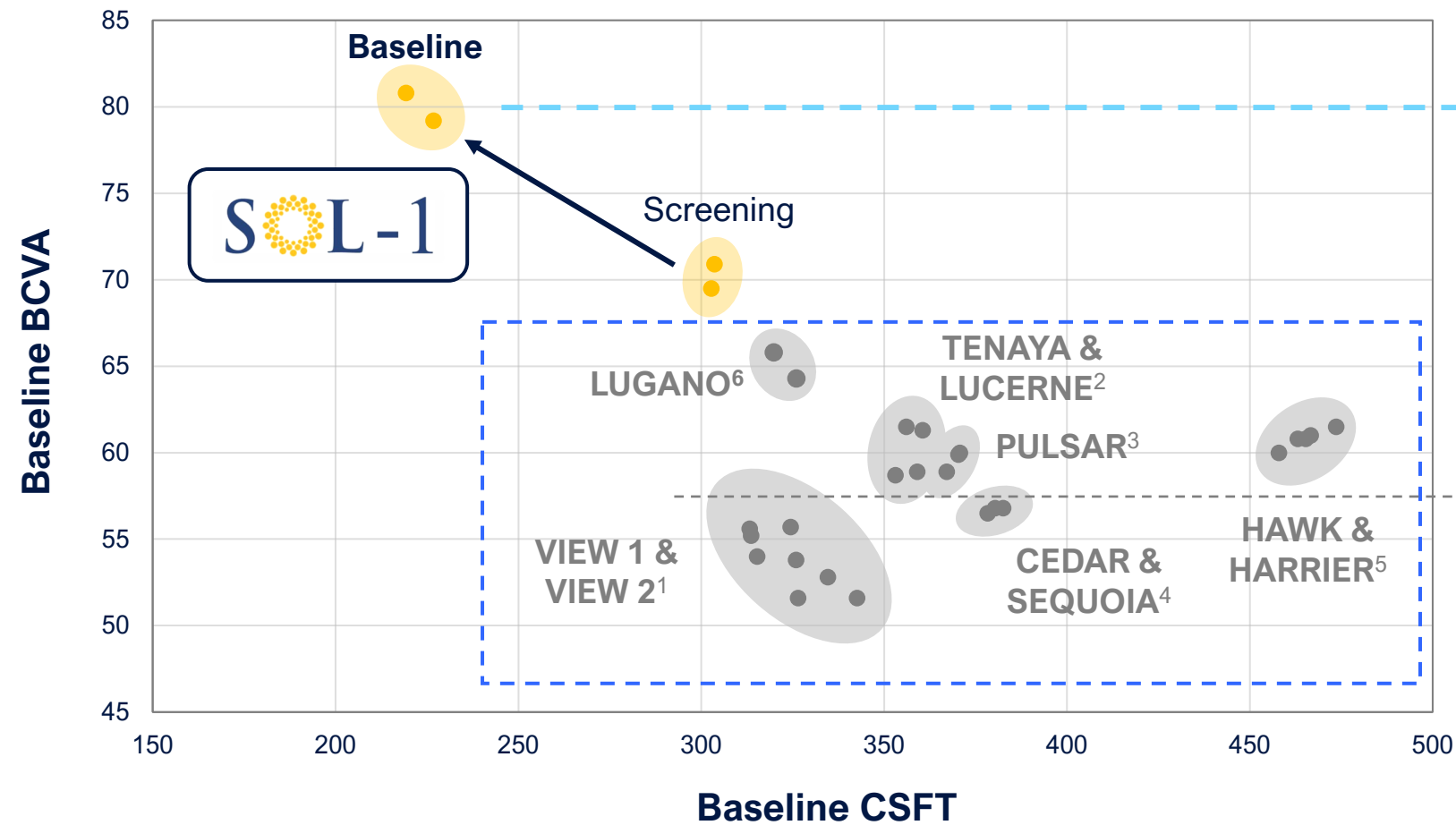


nAMD Trials
mean BCVA: **52 to 66 letters**
(~20/100 to 20/50)

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



Baseline BCVA Across nAMD Trials



SOL-1

mean BCVA: **81 letters (~20/25)**

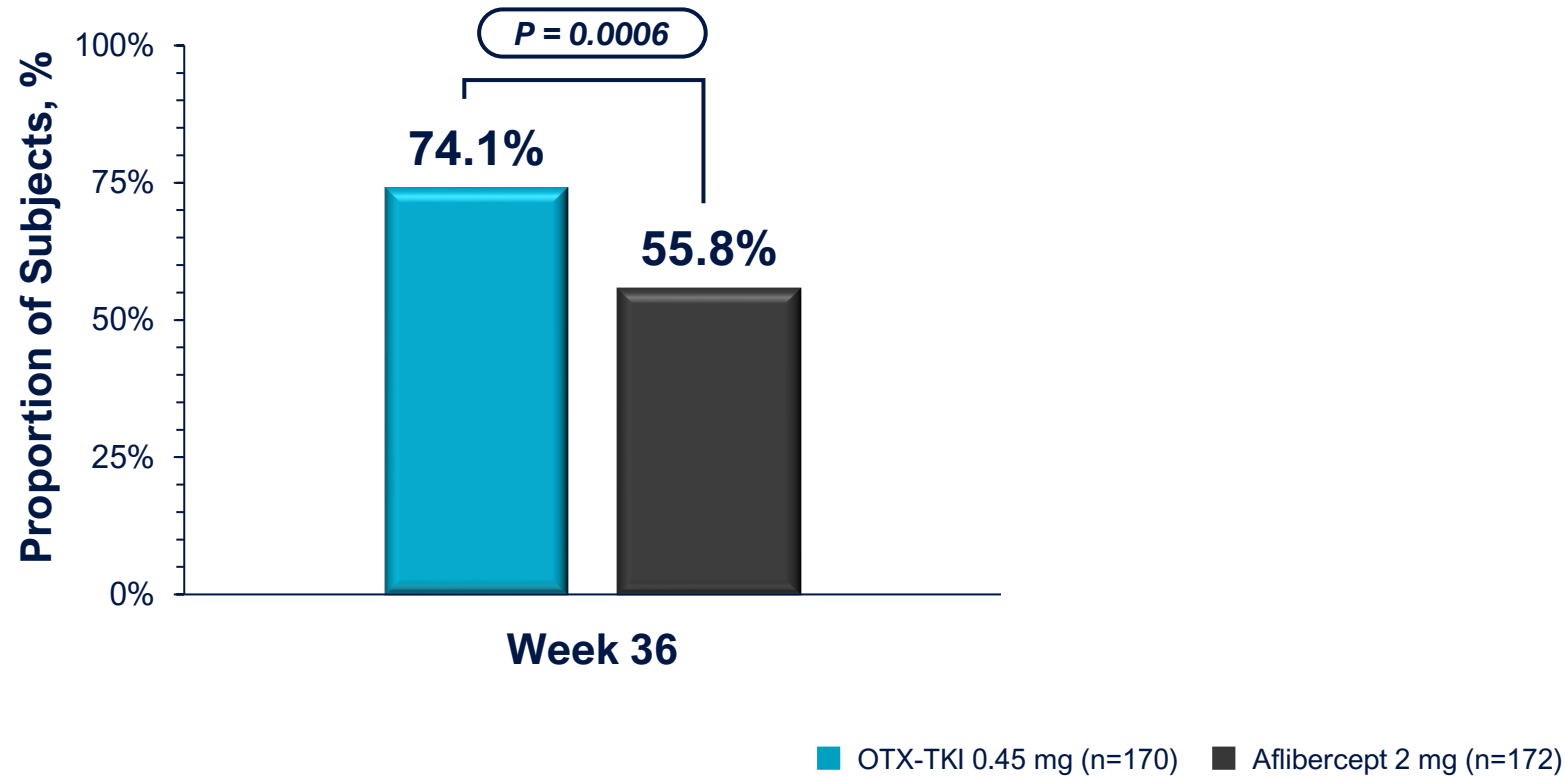
mean CSFT: **219 μ M**

nAMD Trials

mean BCVA: **52 to 66 letters (~20/100 to 20/50)**

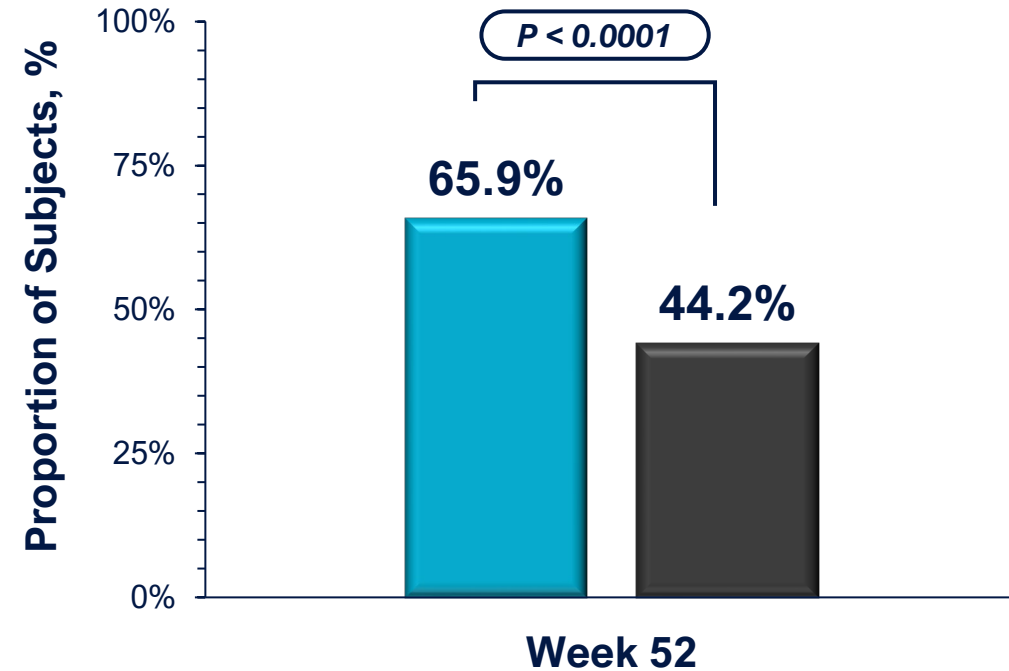
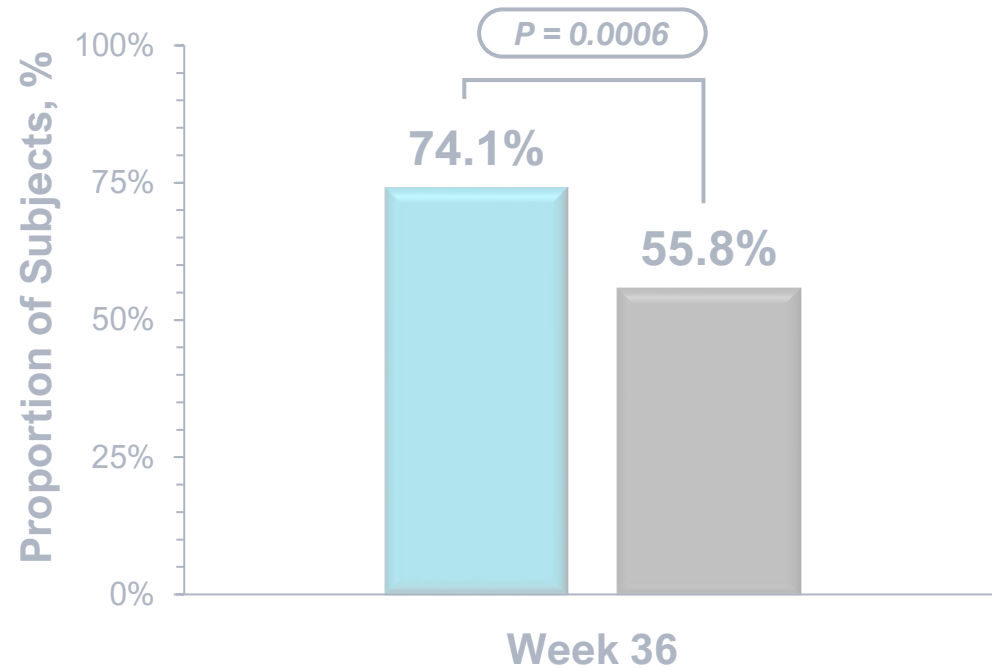
Primary Endpoint Successfully Met

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



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

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

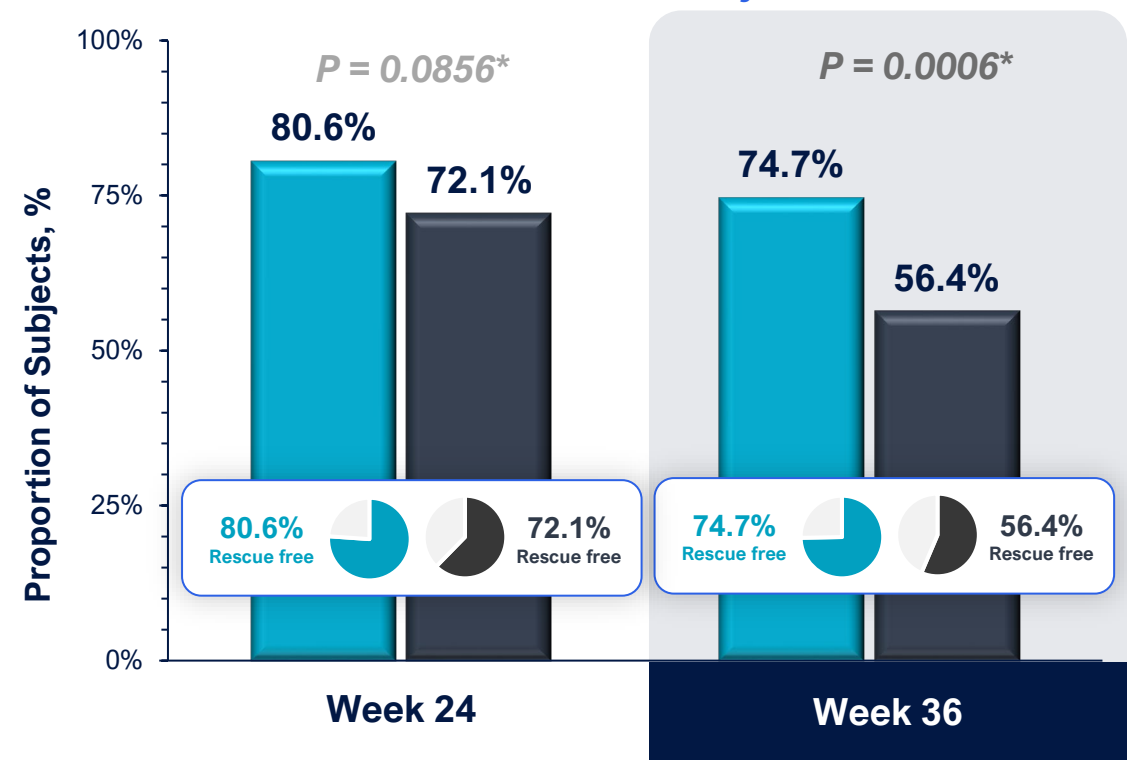


■ OTX-TKI 0.45 mg (n=170) ■ Aflibercept 2 mg (n=172)

Most Subjects (~75%) in the OTX-TKI Arm Did Not Receive Rescue Injections at Week 36

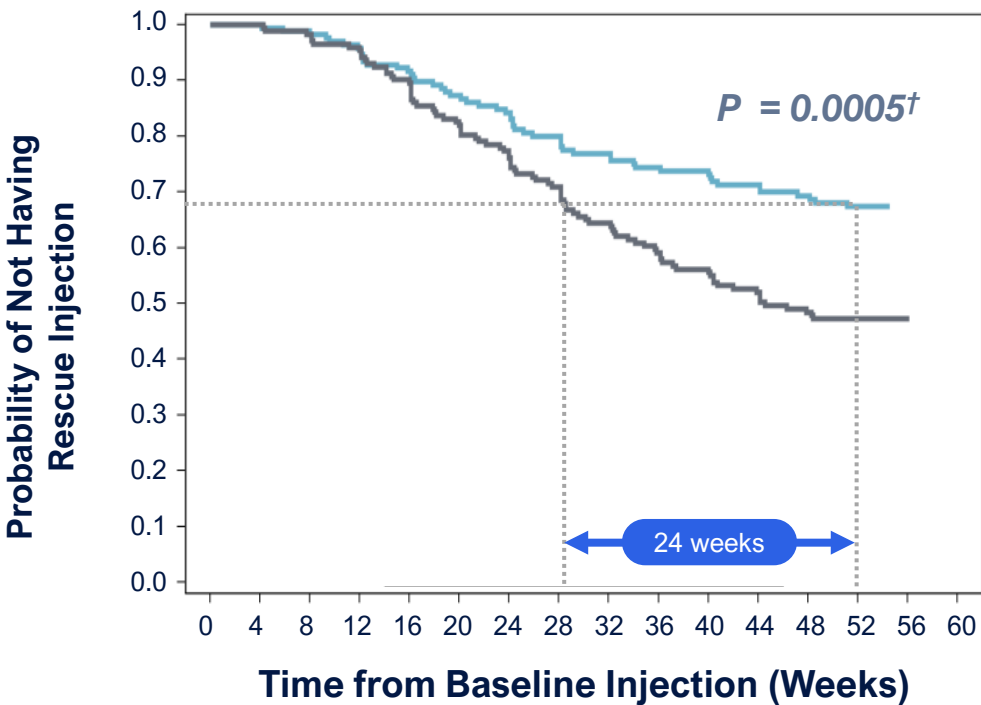
Proportion of Rescue-Free Subjects

Post Hoc Analysis



Time to First Rescue Treatment

Secondary Endpoint



Treatment Burden Reduction vs 2 mg Aflibercept Q8W at ~1 Year

	LOADING DOSES INCLUDED	LOADING DOSES <u>NOT</u> INCLUDED
Faricimab TENAYA/LUCERNE ^{1,2} Phase 3 - to Week 48	14% (6.4 vs 7.4)	45% (2.4 vs 4.4)
Aflibercept 8mg PULSAR ^{3,4} Phase 3 – up to Week 48	29% (5.49 vs 7.7) (weighted mean Q12 and Q16 arms)	47% (2.49 vs 4.7) (weighted mean Q12 and Q16 arms)
4D-150 PRISM ⁵ Phase 2b (3E10 dose)* - through Week 52	50% (3.97 vs 8) vs projected on-label aflibercept 2 mg control	51% (2.97 vs 6) vs projected on-label aflibercept 2 mg control
ADVM-022 LUNA ⁶ Phase 2 (2E11 dose)*	65% (2.8 vs 8) vs projected on-label aflibercept 2 mg control	70% (1.8 vs 6) vs projected on-label aflibercept 2 mg control
RGX-314 Subretinal Phase 2 Study ^{7,8} (Low dose/High dose annualized) [†]	58 - 60% (3.2/3.4 vs 8) vs projected on-label aflibercept 2 mg control	60 - 63% (2.2/2.4 vs 6) vs projected on-label aflibercept 2 mg control
EYP-1901 2.7mg LUGANO ⁹ Phase 3 – up to Week 56	27% (6.1 vs 8.3)	42% (3.1 vs 5.3)
OTX-TKI Post hoc analysis of estimated treatment burden reduction in SOL-1 Phase 3 (using SOL-R supplemental injection criteria)	56% (3.95 vs 9) [‡] vs projected on-label aflibercept 2 mg control	72% (1.95 vs 7) vs projected on-label aflibercept 2 mg control

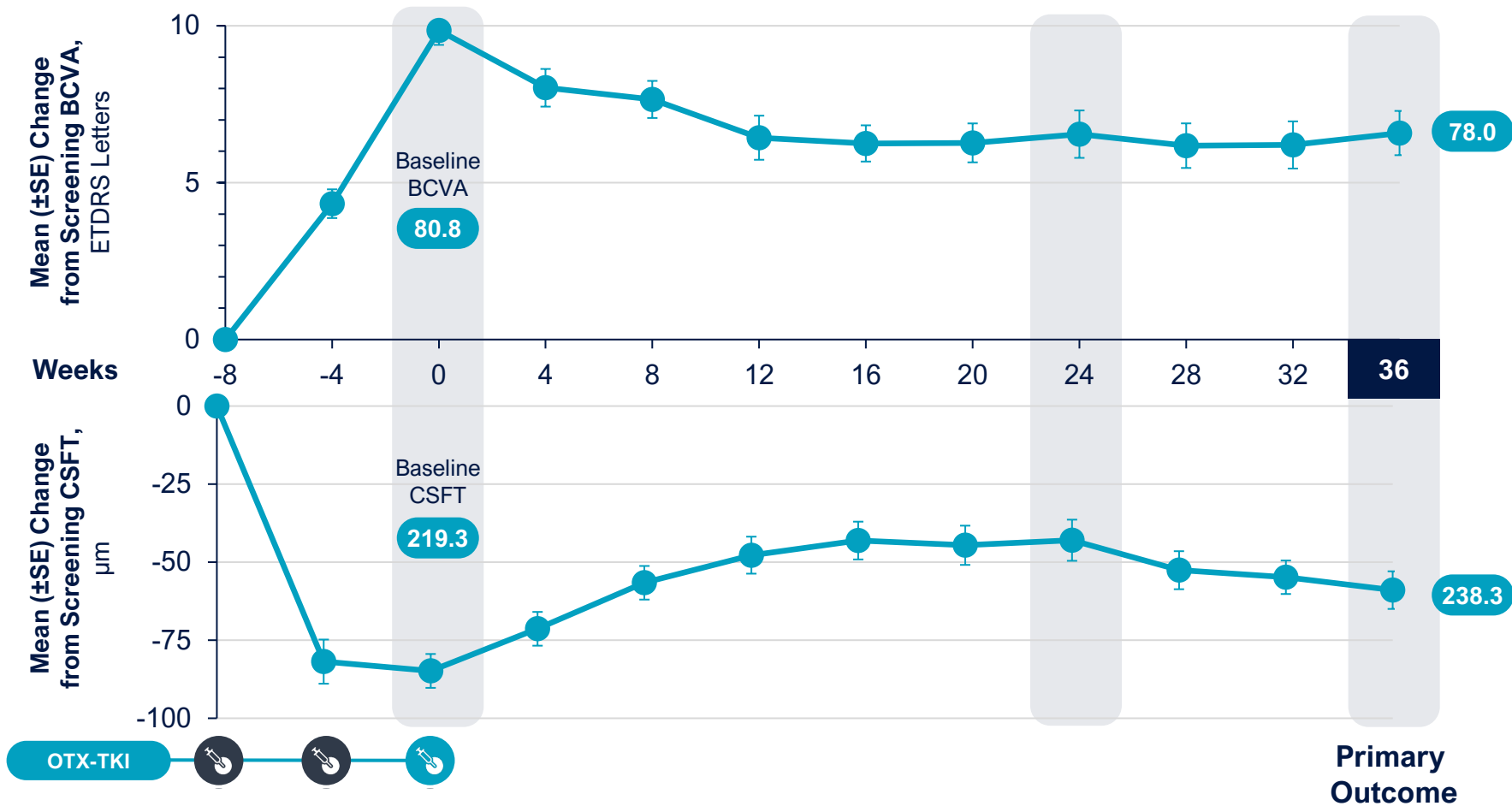
*Previously treated wet age-related macular degeneration population; † Does not include the subretinal surgery as a treatment; ‡ OTX-TKI durability measured over 60 weeks to include loading doses at Week-8 and Week-4.

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

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



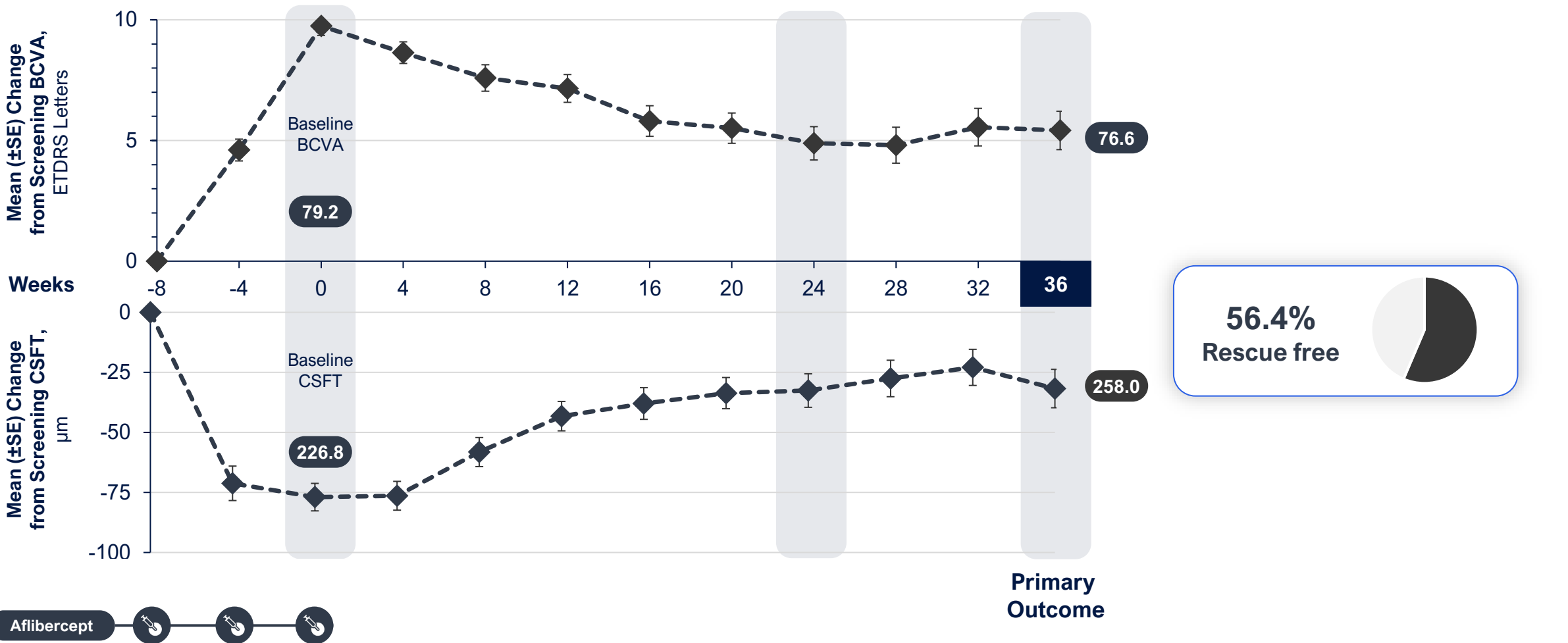
Post Hoc Analysis: Mean Change in BCVA and CSFT from Screening



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

SOL-1

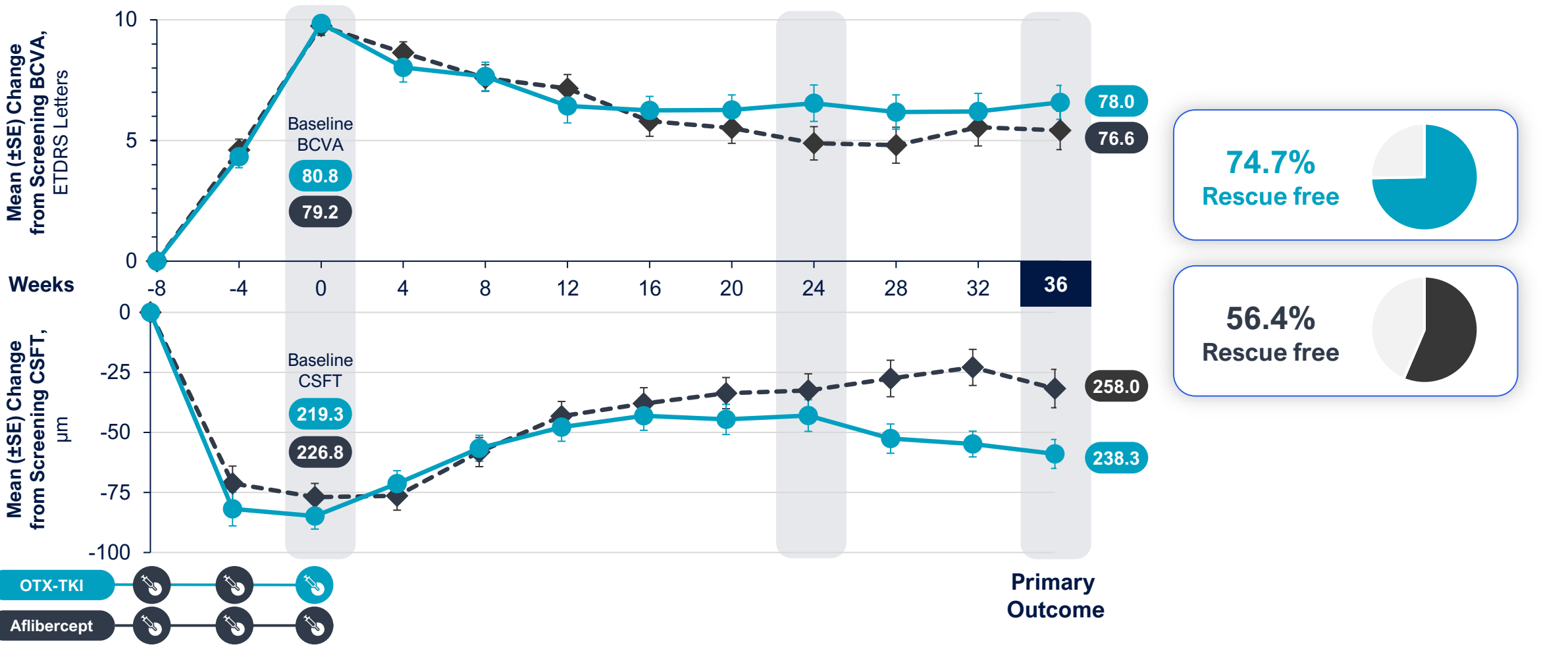
Post Hoc Analysis: Mean Change in BCVA and CSFT from Screening



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

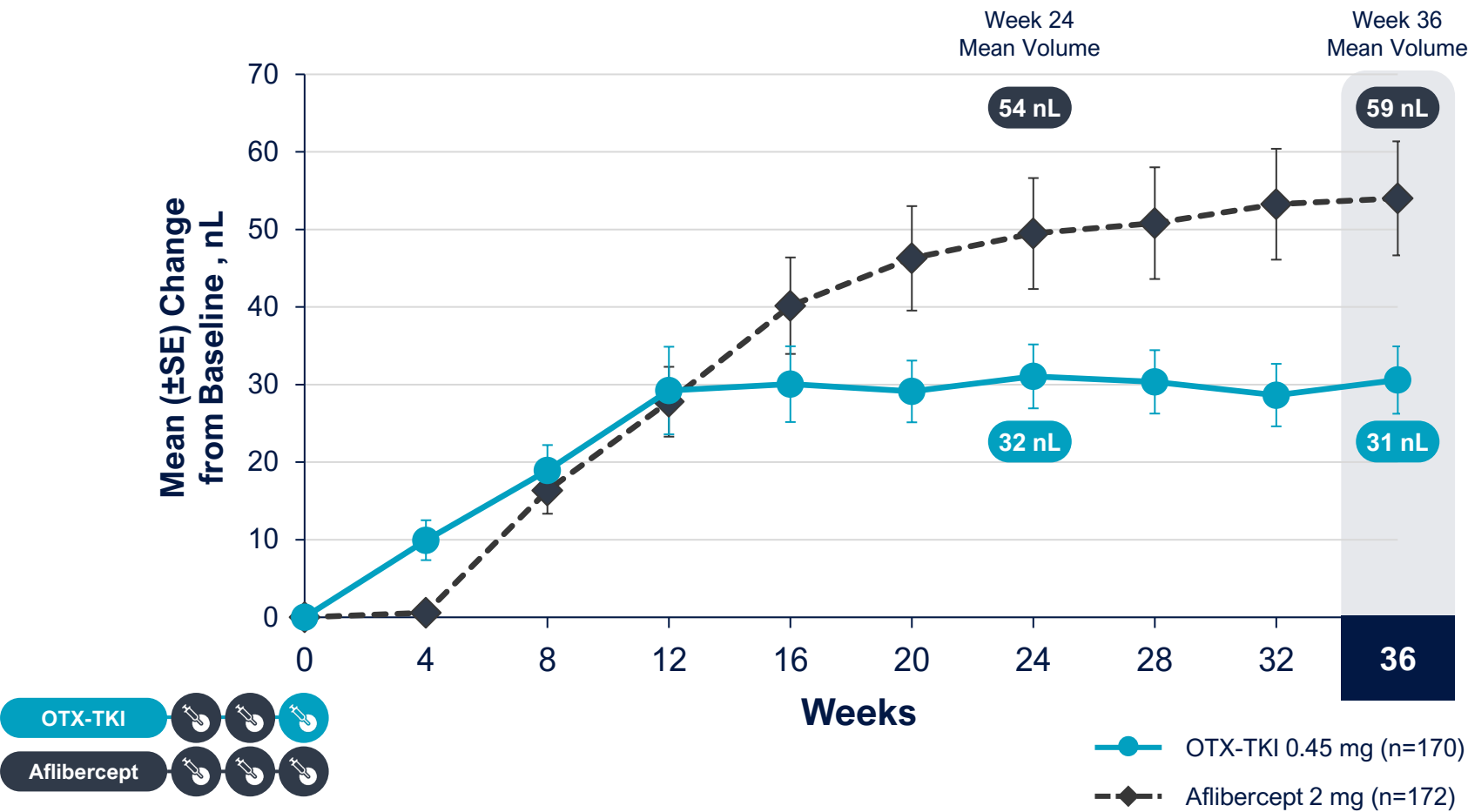
SOL-1

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

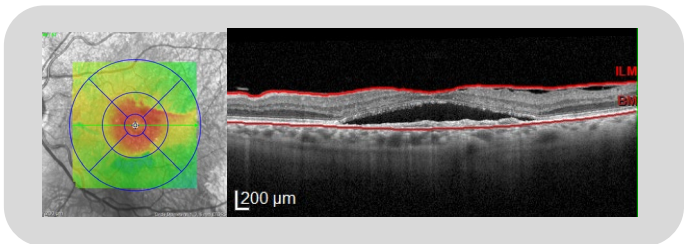


OTX-TKI Delivered Sustained Fluid Control

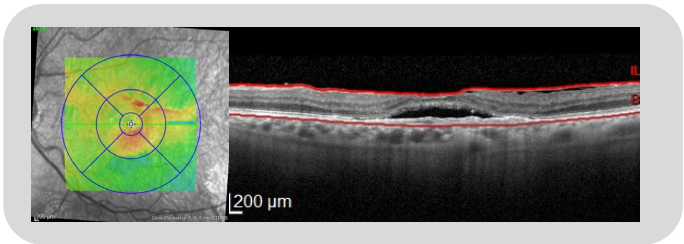
Prespecified Exploratory Analysis: Mean Change in Intra-Retinal and Sub-Retinal Fluid Volume



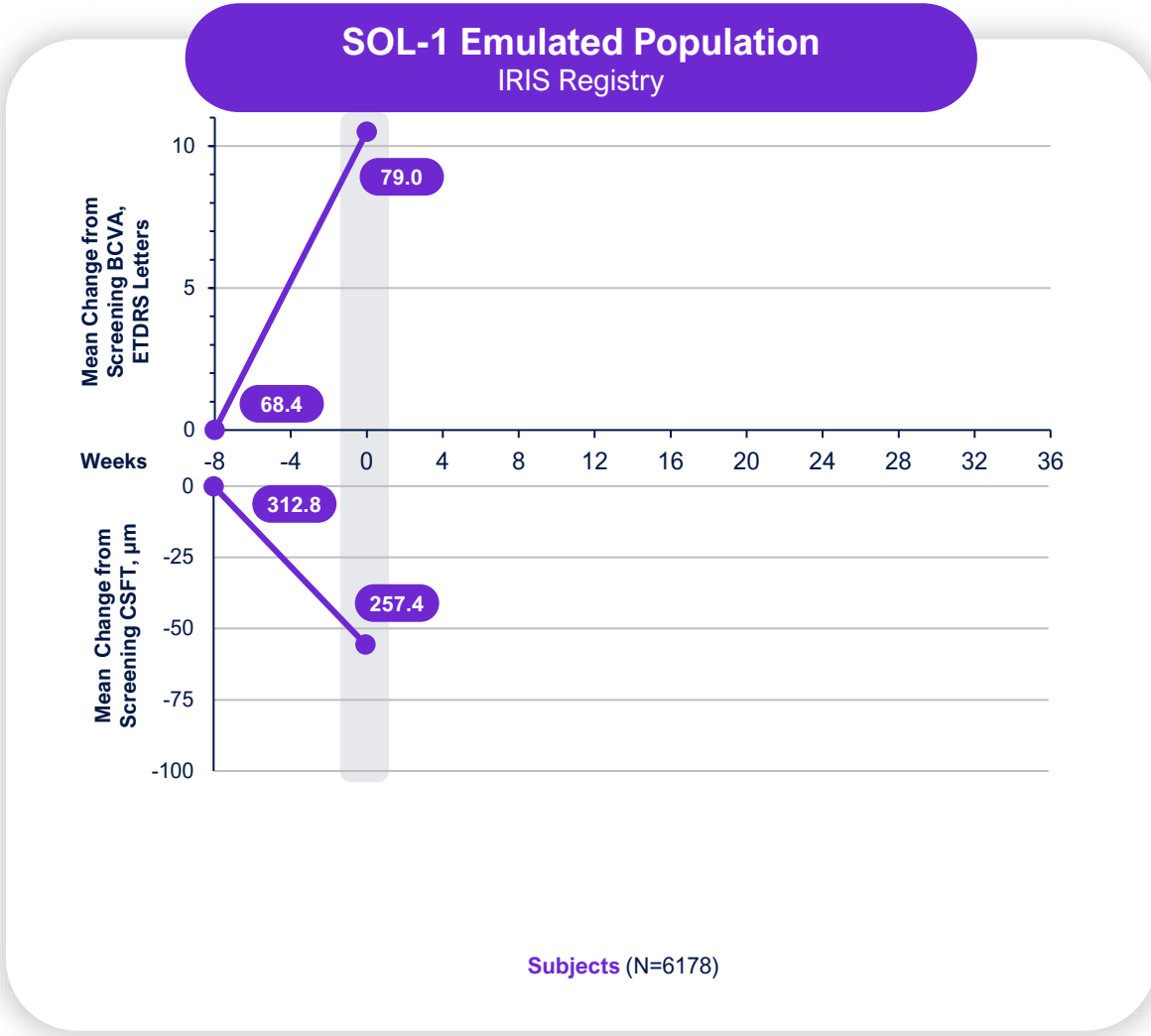
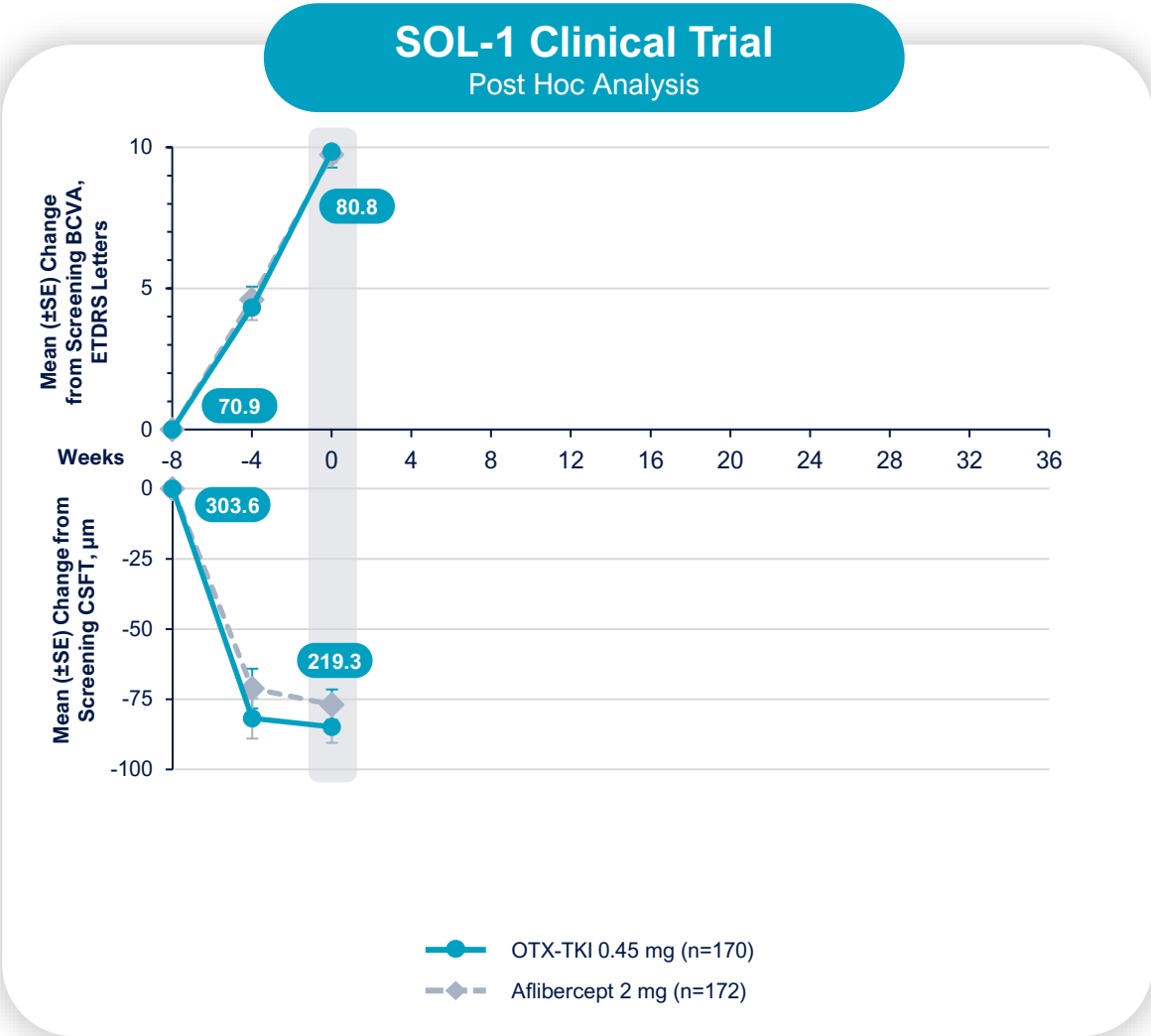
Total Fluid Volume: 60 nL



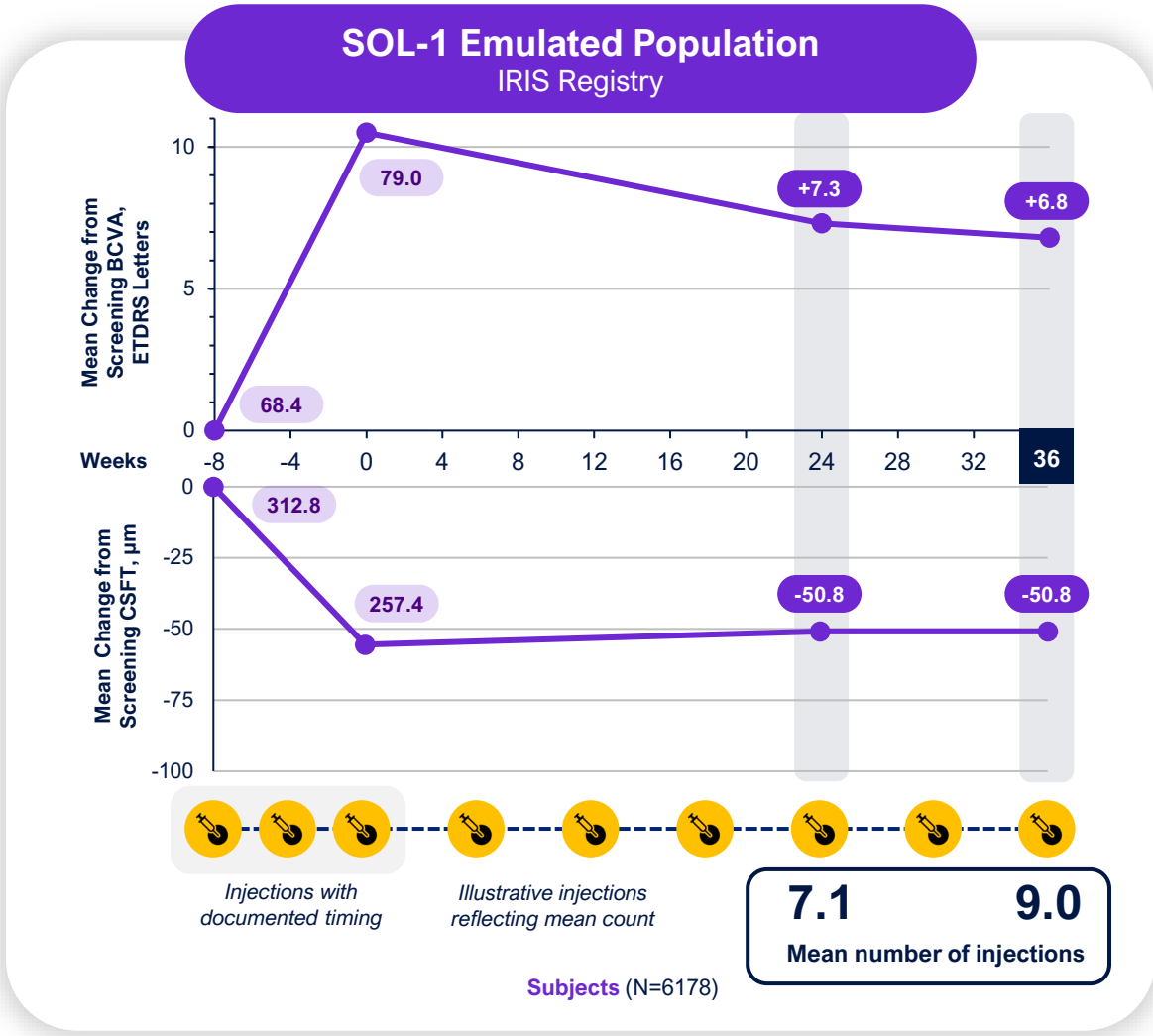
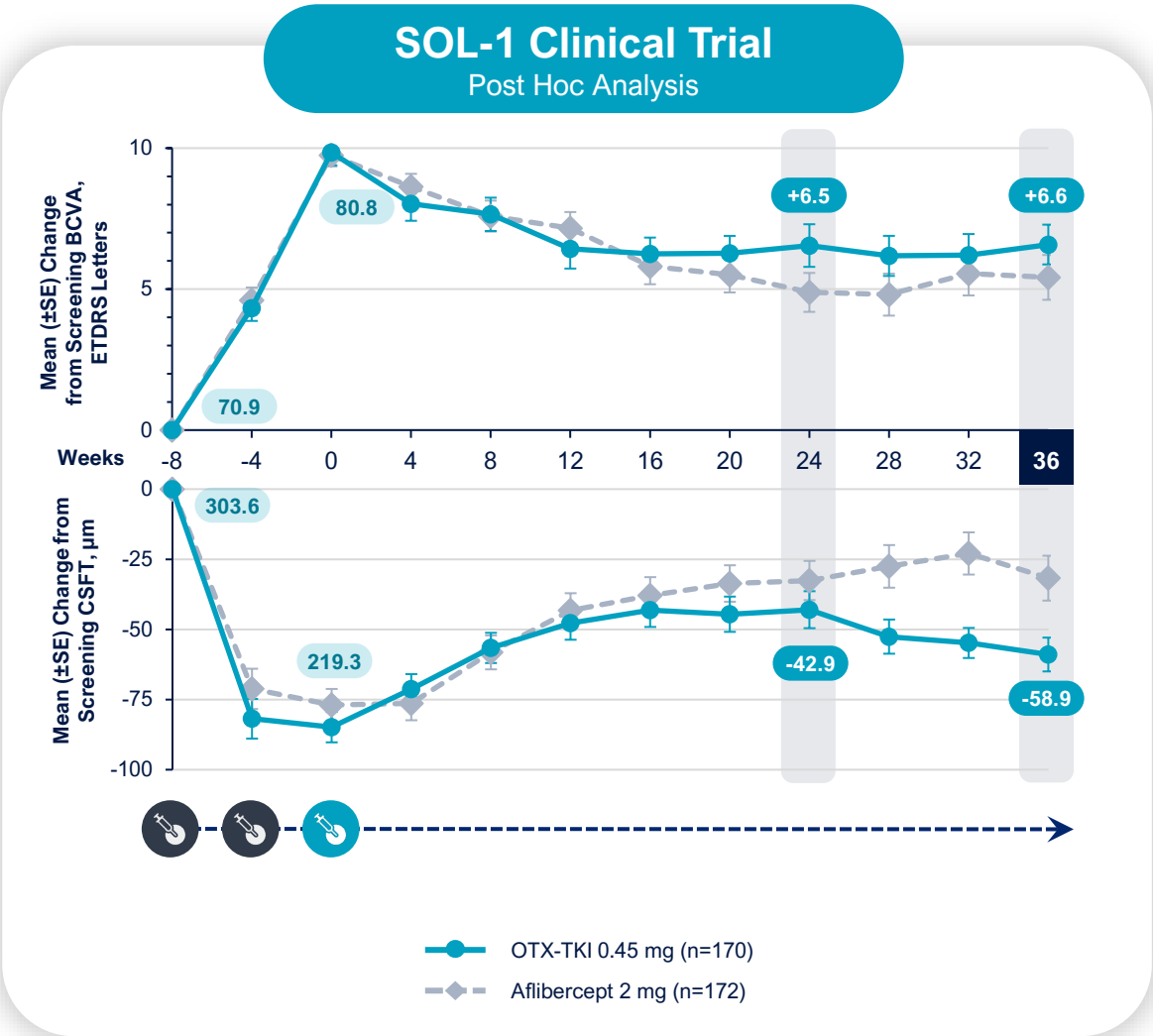
Total Fluid Volume: 30 nL



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



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



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

OTX-TKI was Generally Well Tolerated

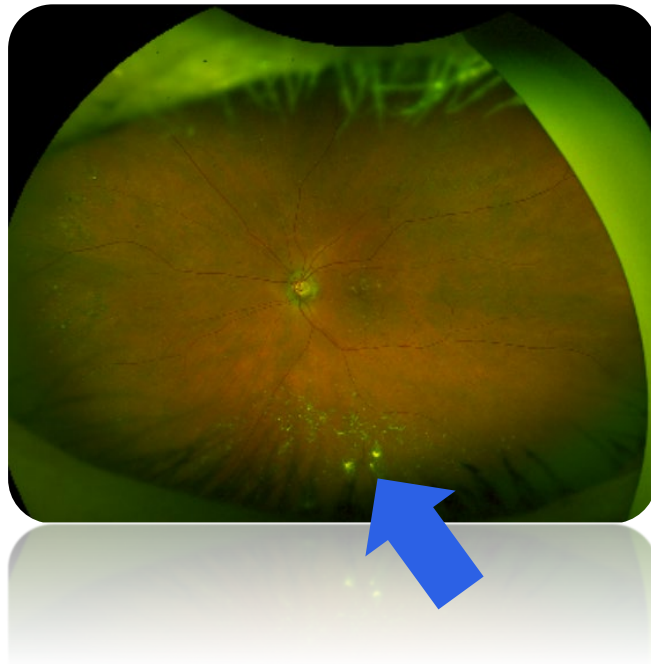
Ocular Adverse Events in the Study Eye

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**

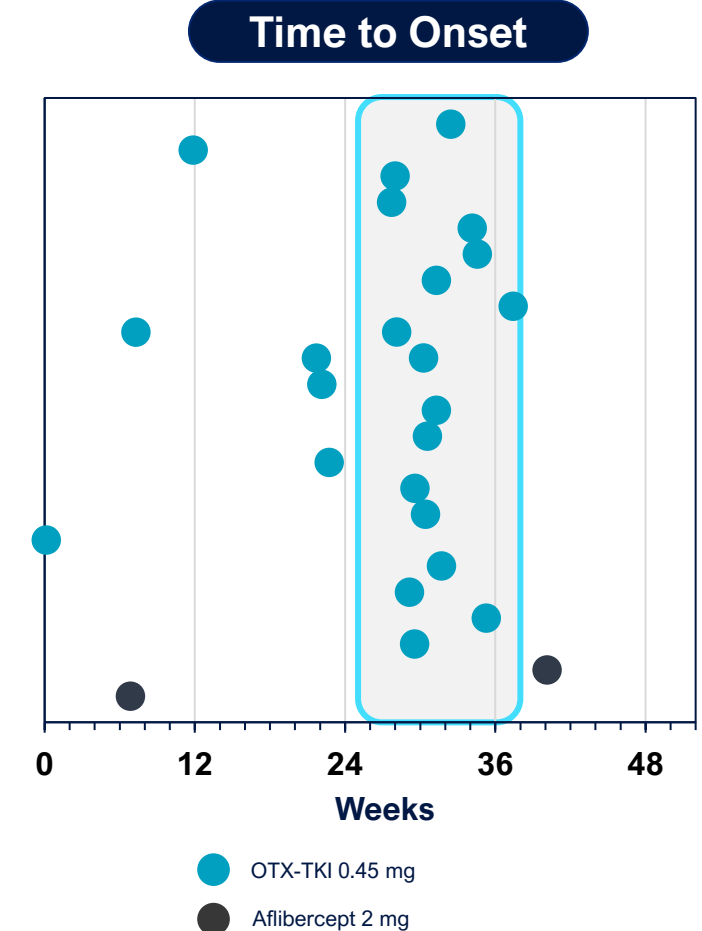
Appearance of Floaters May Correspond to Hydrogel Dissolution and Drug Elution

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

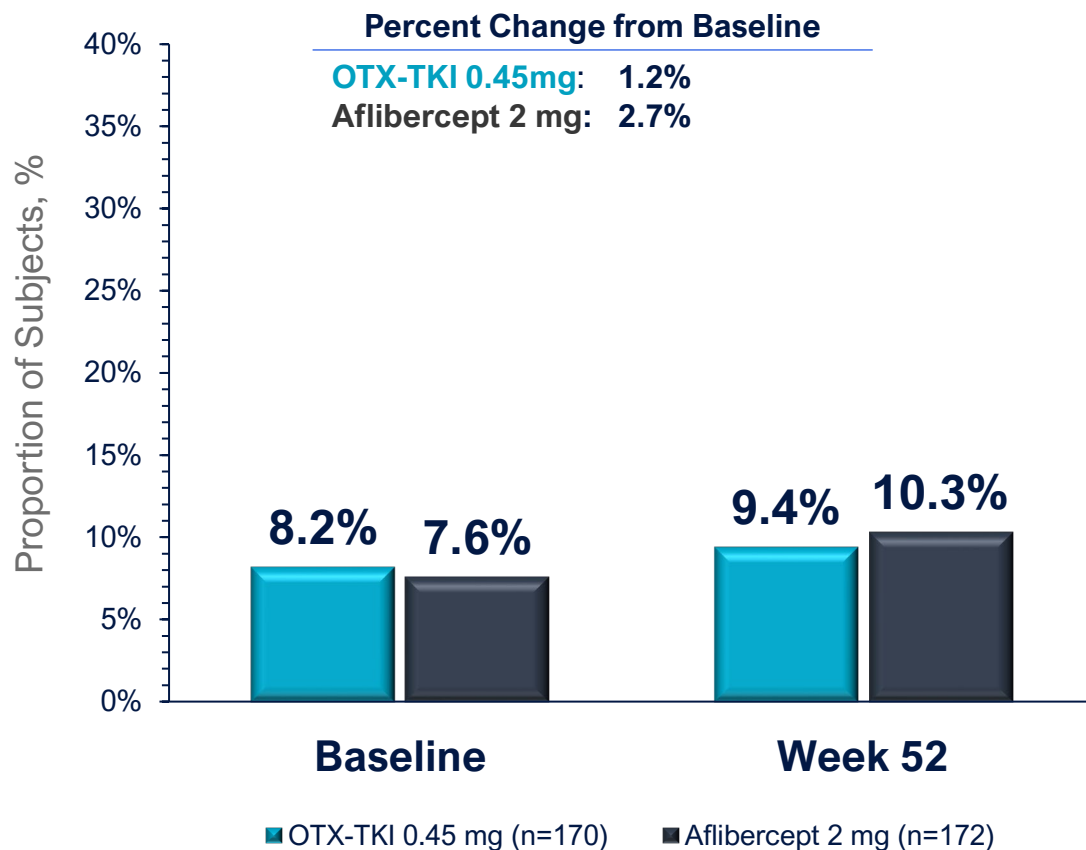
- All cases were mild to moderate in severity
- No evidence of IOI associated with floaters
- Onset of vitreous floaters AE coincides with drug elution stage of OTX-TKI hydrogel bioresorption process
- **For all subjects with vitreous floaters AE reported, drug particles are no longer visible**



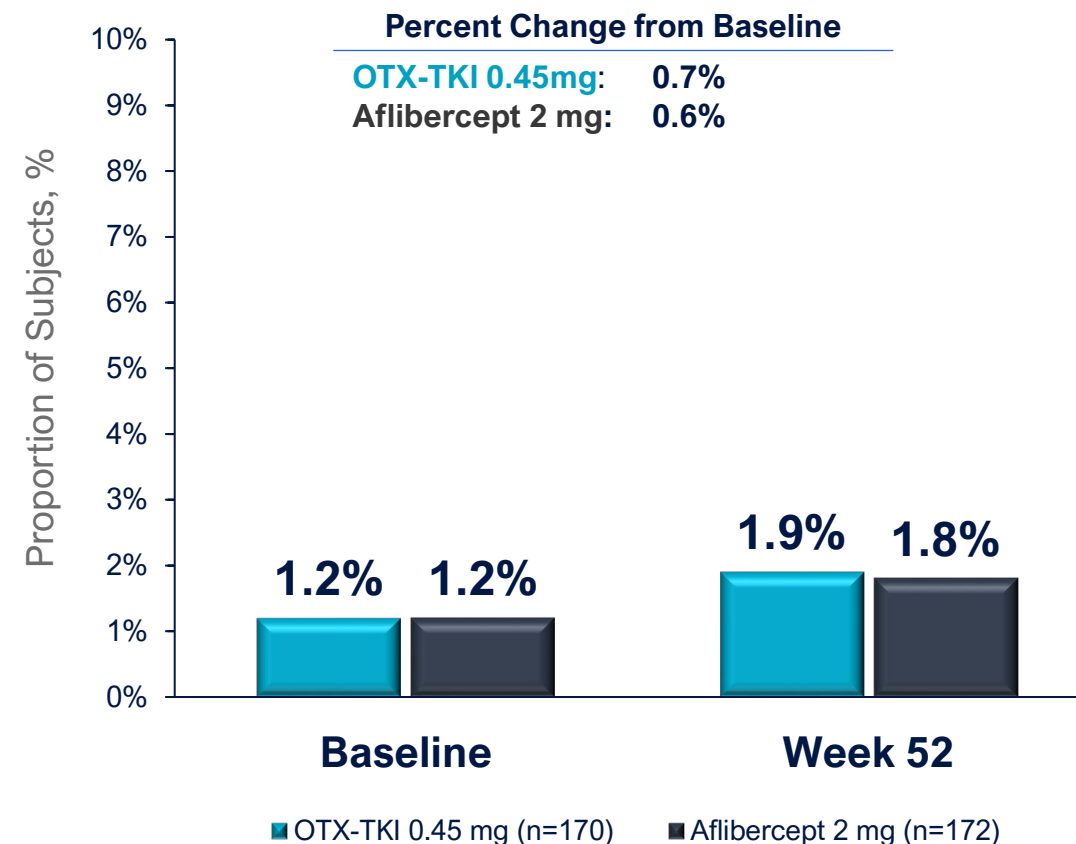
Incidence of Macular Atrophy in SOL-1

Safety Analysis

Any Macular Atrophy¹



Macular Atrophy in the Central 1mm¹



Superiority Primary Endpoint Successfully Met

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

First trial to demonstrate durability ≥ 9 months

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

Unmatched Durability

Visual and anatomic stability with OTX-TKI

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

Sustained Disease Control

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

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

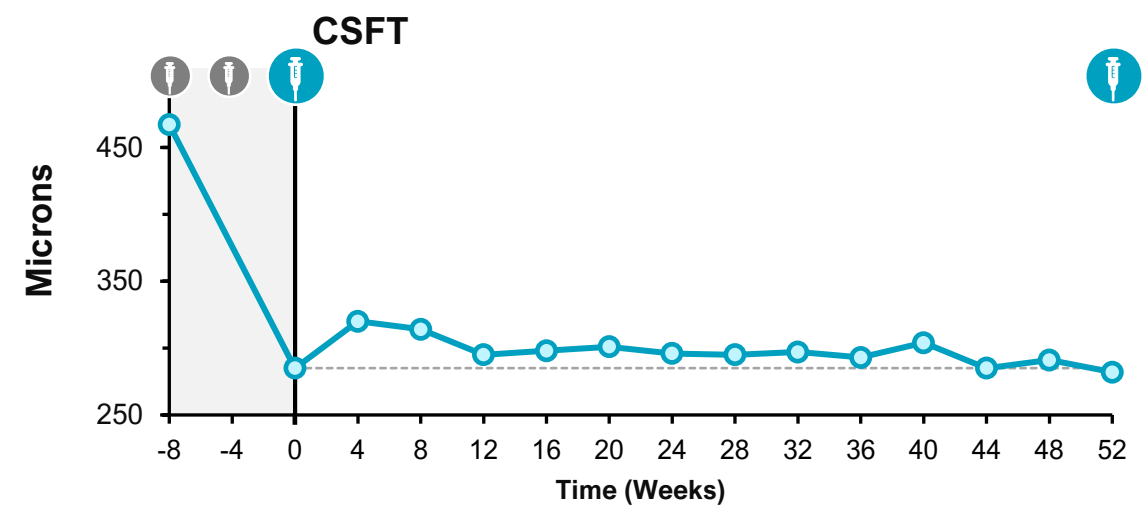
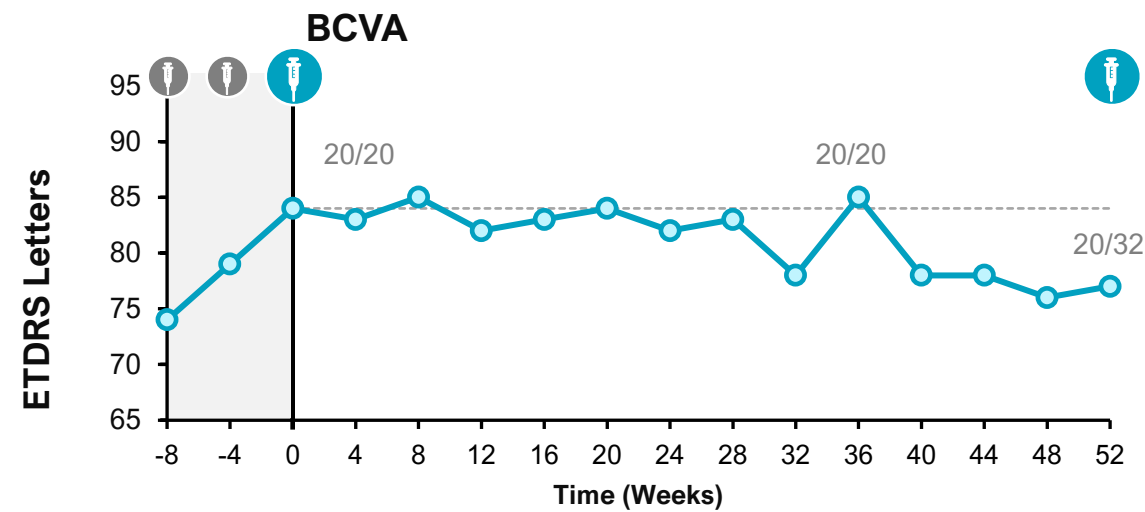
Well-Tolerated

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

SOL-1 Clinical Evidence

Mark R. Barakat, MD, FASRS

OTX-TKI Case 1



Screening Aflibercept (2mg)

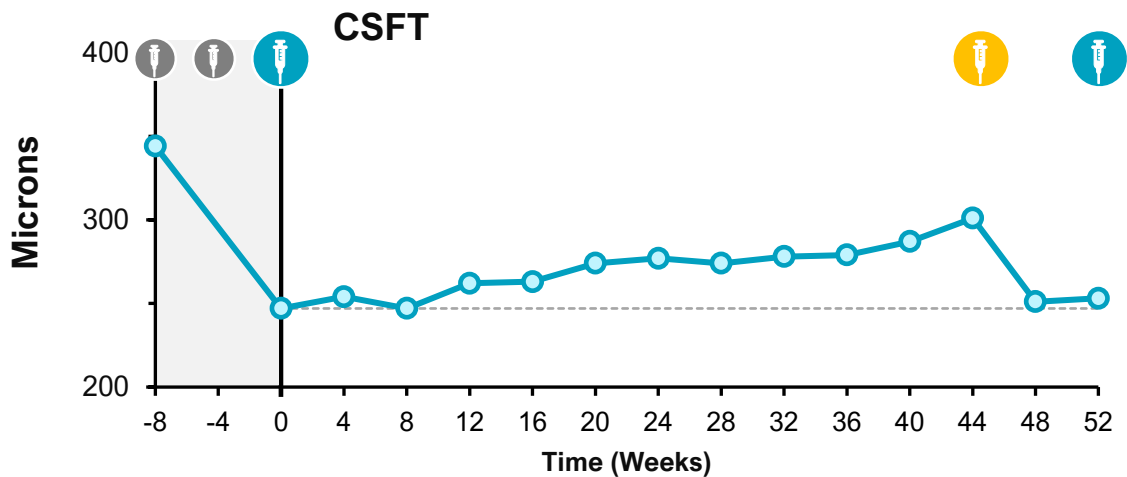
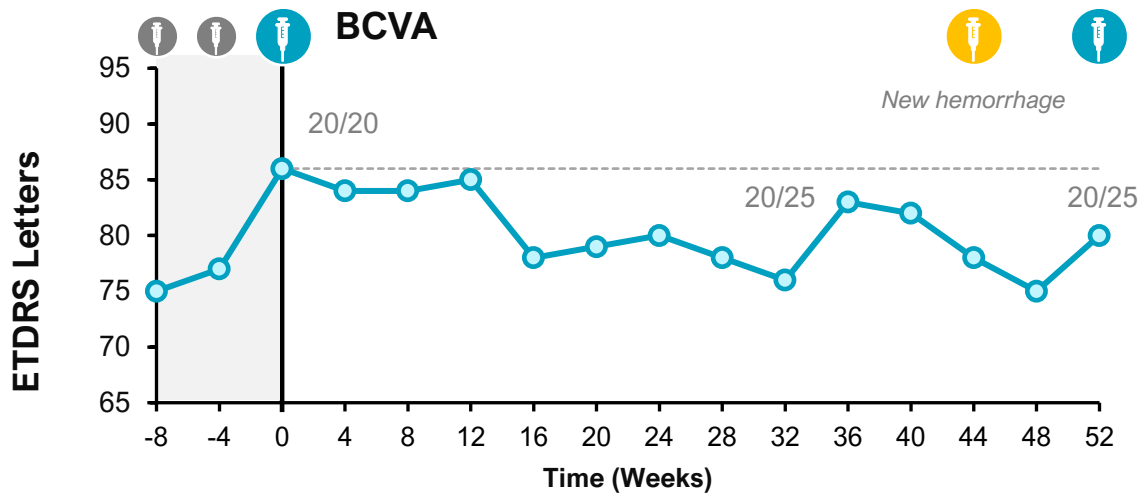
OTX-TKI (0.45mg)

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

-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	

OTX-TKI Case 2

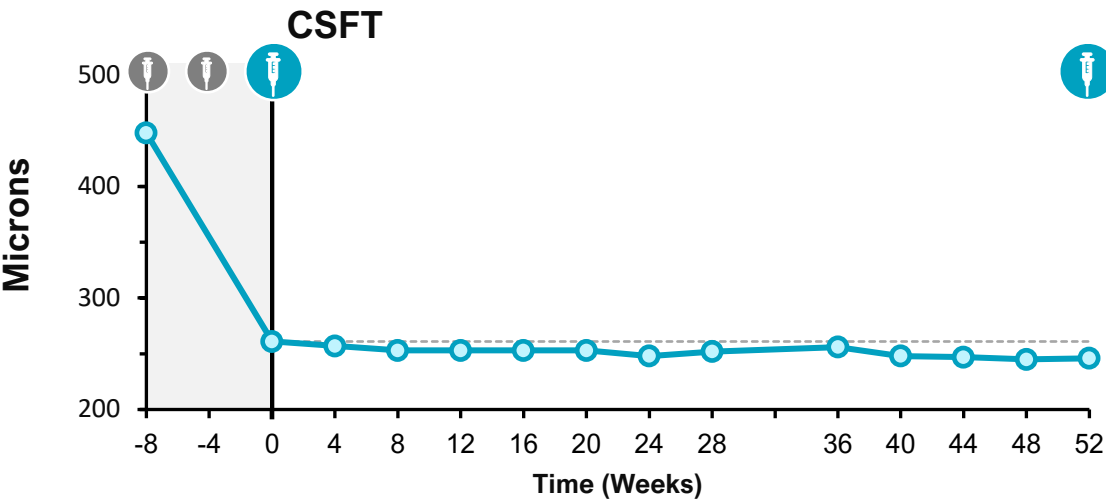
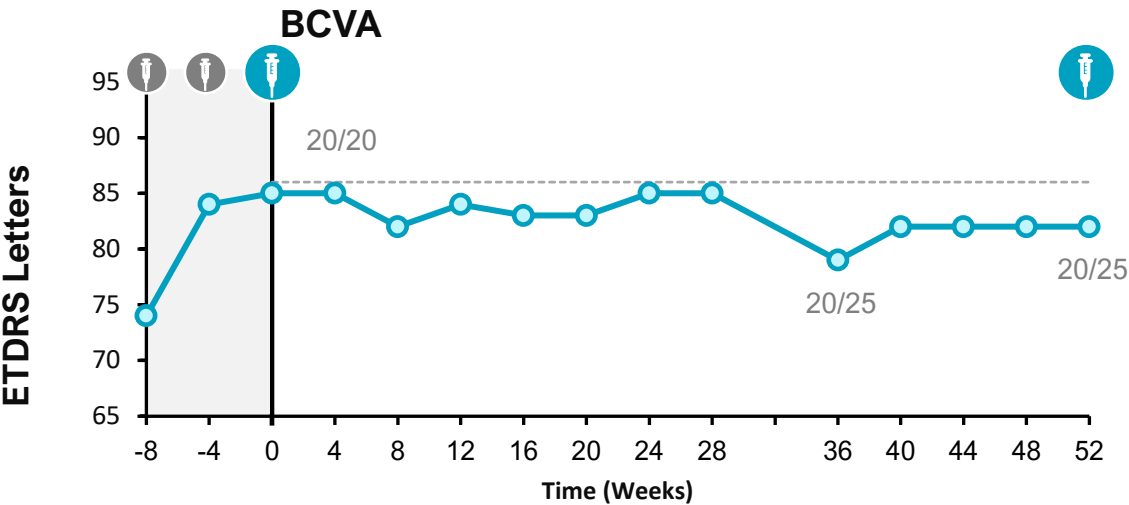


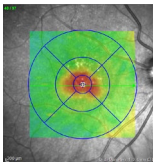
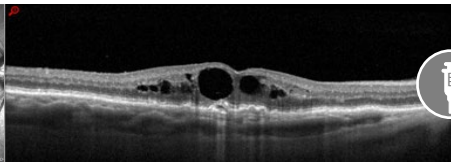
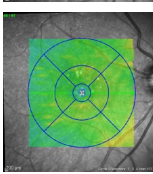
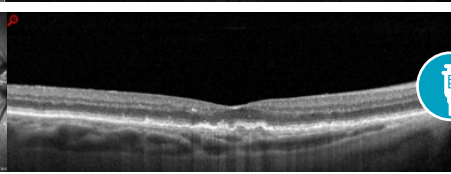
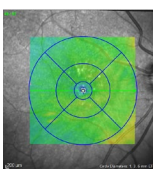
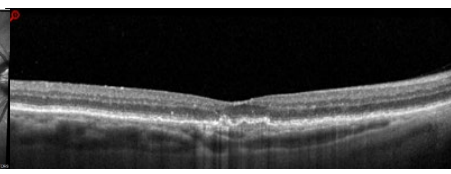
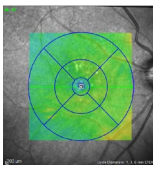
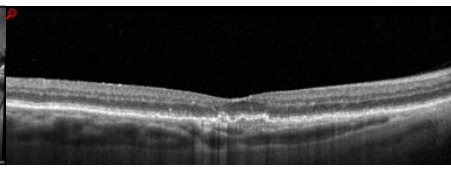
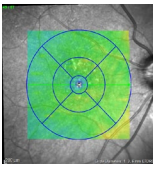
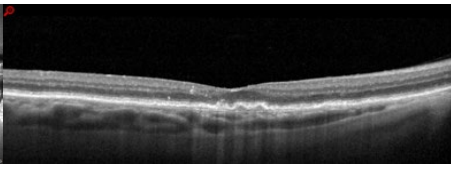
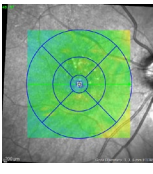
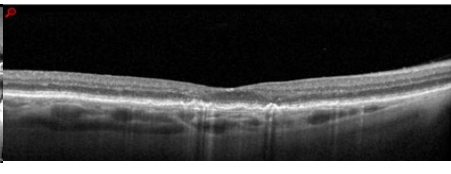
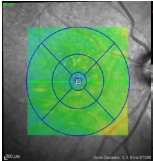
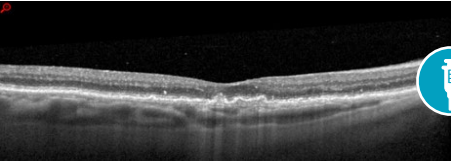
- Screening Aflibercept (2mg)
- OTX-TKI (0.45mg)
- Per-Protocol Rescue Aflibercept (2mg)

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

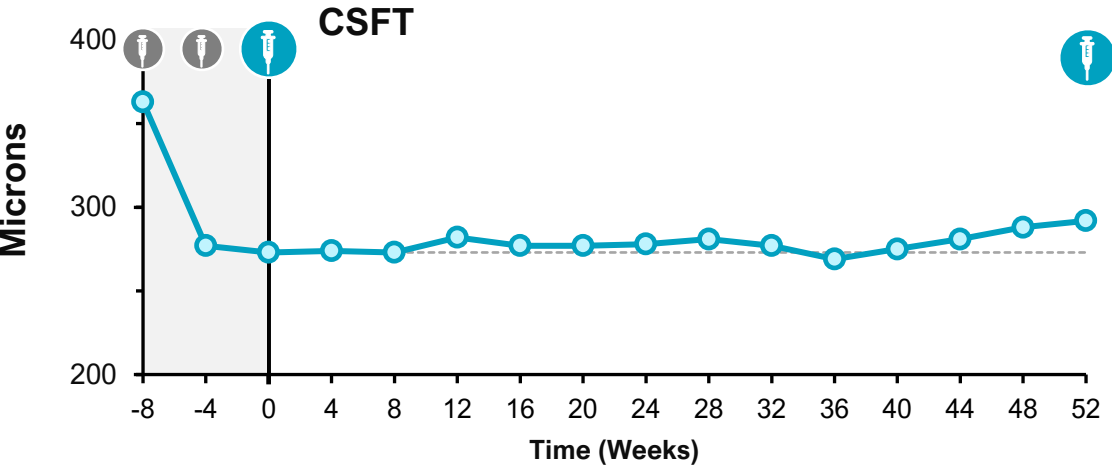
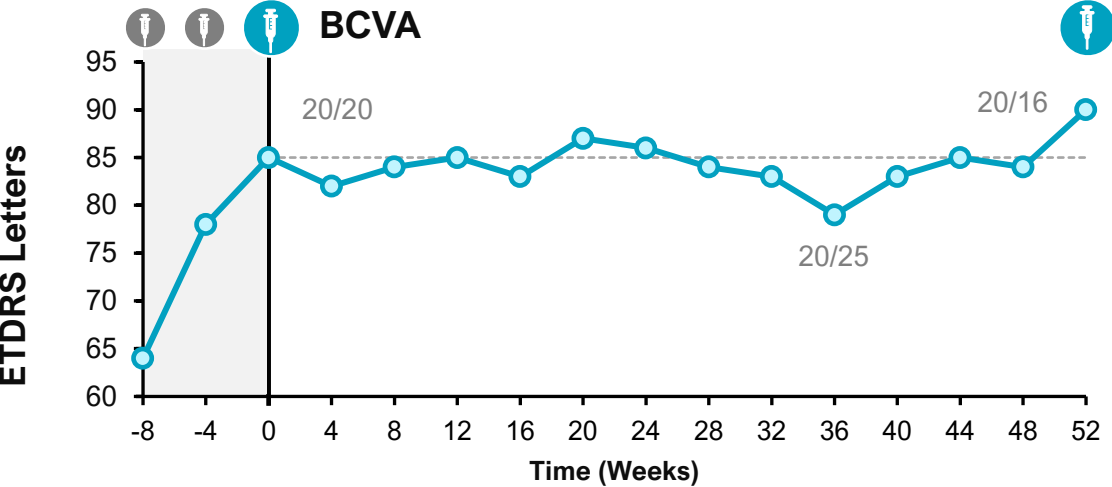
-8 Weeks	BCVA: 75 Ltrs CSFT: 344 µm	
Baseline	BCVA: 86 Ltrs Snellen: 20/20 CSFT: 247 µm	
Week 4	BCVA (Δ): 84 (-2) Ltrs CSFT (Δ): 254 (+7) µm	
Week 12	BCVA (Δ): 85 (-1) Ltrs CSFT (Δ): 262 (+15) µm	
Week 24	BCVA (Δ): 80 (-6) Ltrs CSFT (Δ): 277 (+30) µm	
Week 36	BCVA (Δ): 83 (-3) Ltrs Snellen: 20/25 CSFT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

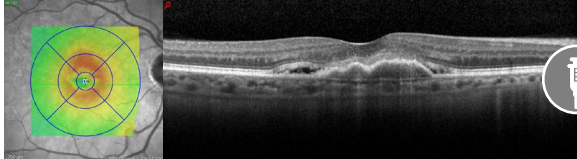
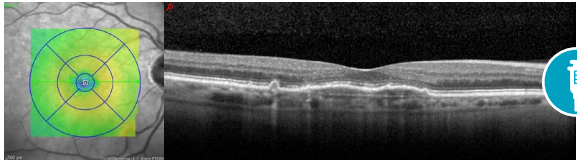
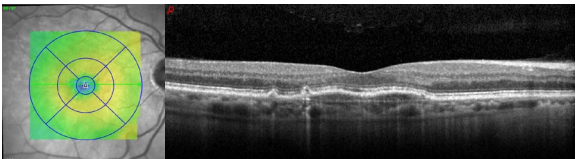
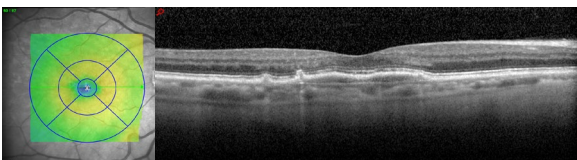
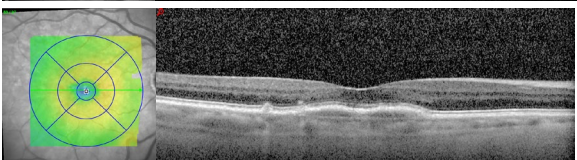
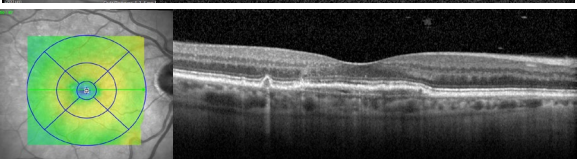
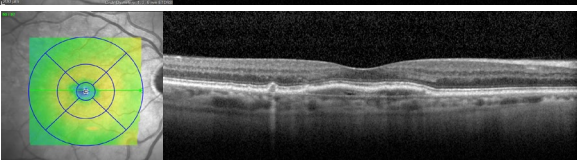
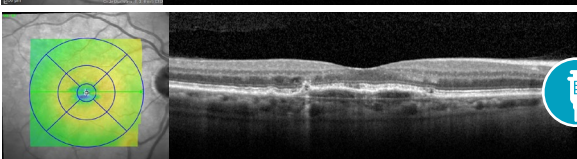
OTX-TKI Case 3



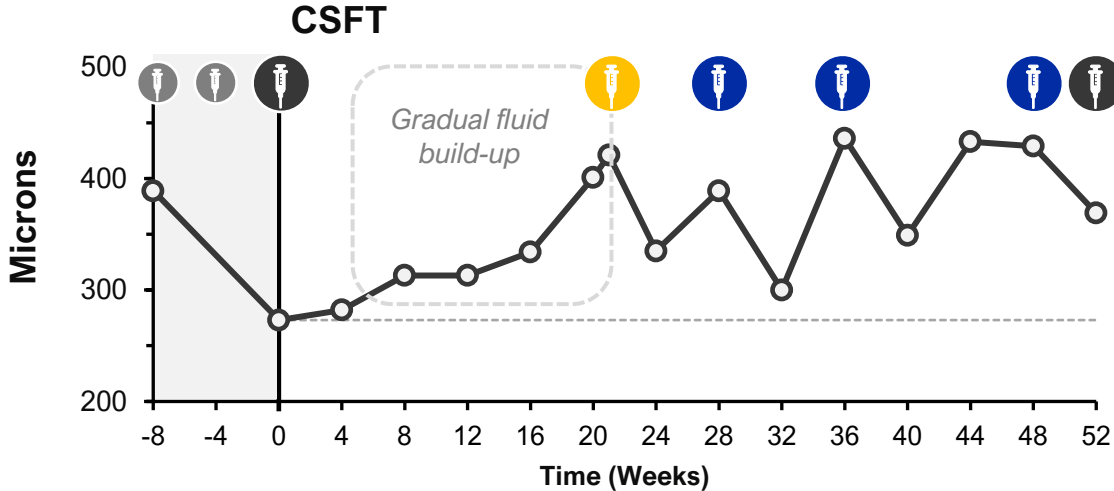
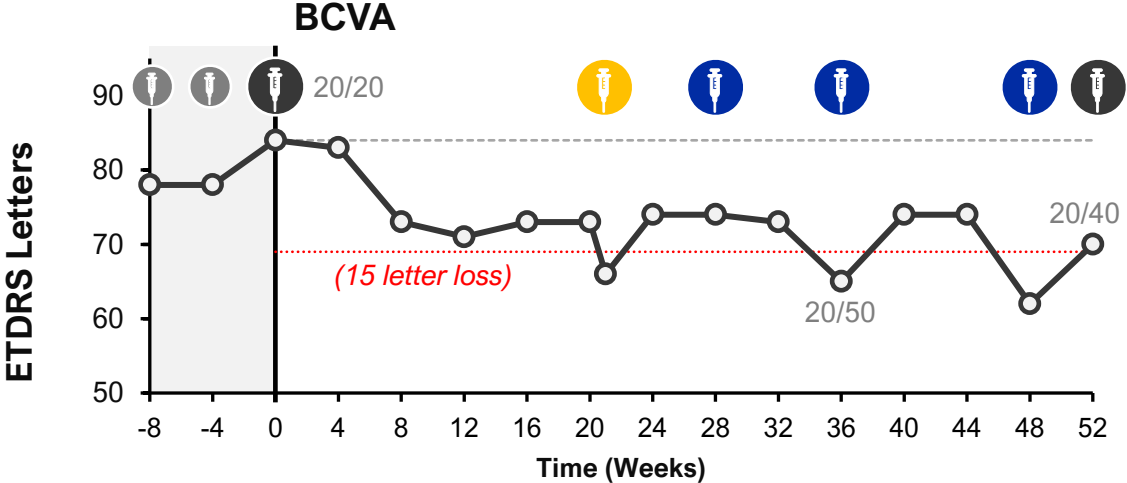
-8 Weeks	BCVA: 74 Ltrs CSFT: 448 µm	 
Baseline	BCVA: 85 Ltrs Snellen: 20/20 CSFT: 261 µm	 
Week 4	BCVA (Δ): 85 (0) Ltrs CSFT (Δ): 257 (-4) µm	 
Week 12	BCVA (Δ): 84 (-1) Ltrs CSFT (Δ): 253 (-8) µm	 
Week 24	BCVA (Δ): 85 (0) Ltrs CSFT (Δ): 248 (-13) µm	 
Week 36	BCVA (Δ): 79 (-6) Ltrs Snellen: 20/25 CSFT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

OTX-TKI Case 4



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

Aflibercept Case 1



- Screening Aflibercept (2mg)
- Study Aflibercept (2 mg)
- Per-Protocol Rescue Aflibercept (2mg)
- Investigator Discretion Rescue



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

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

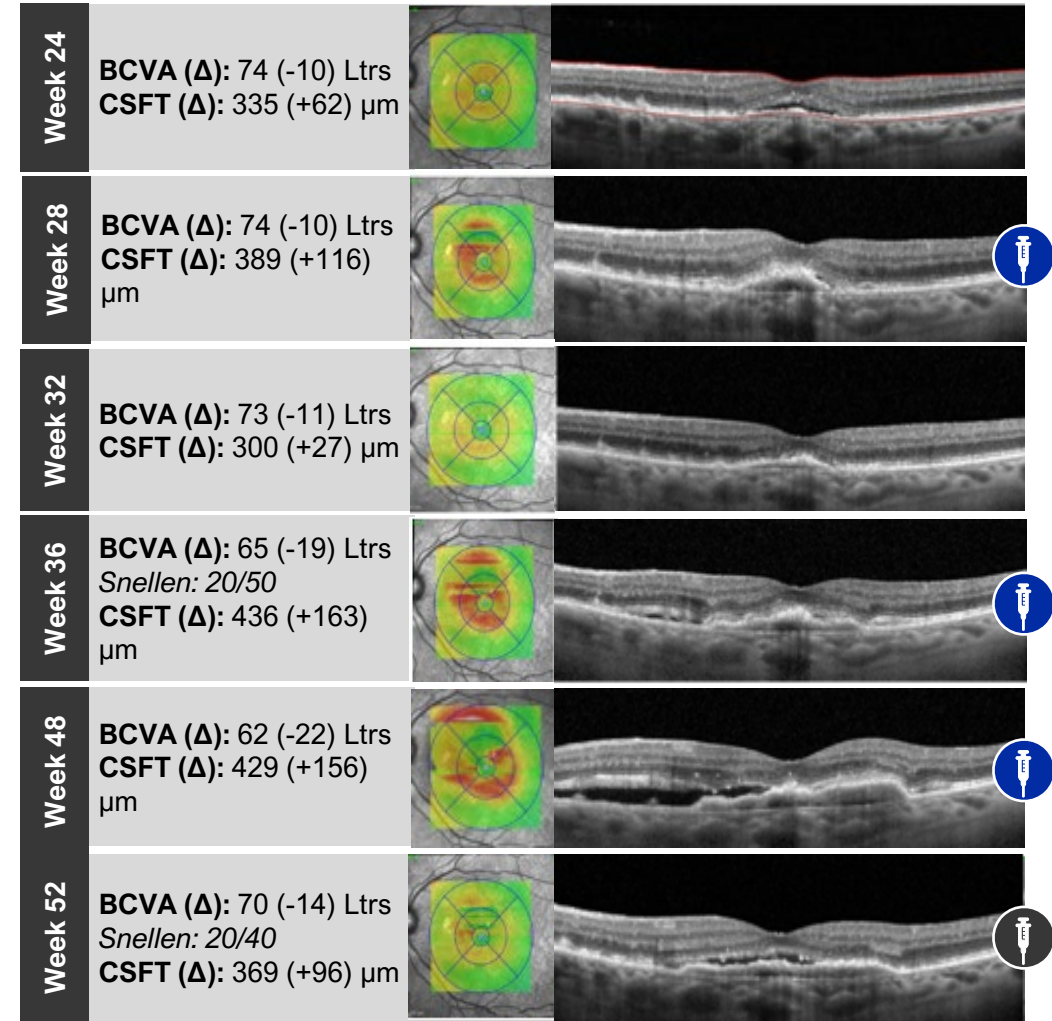
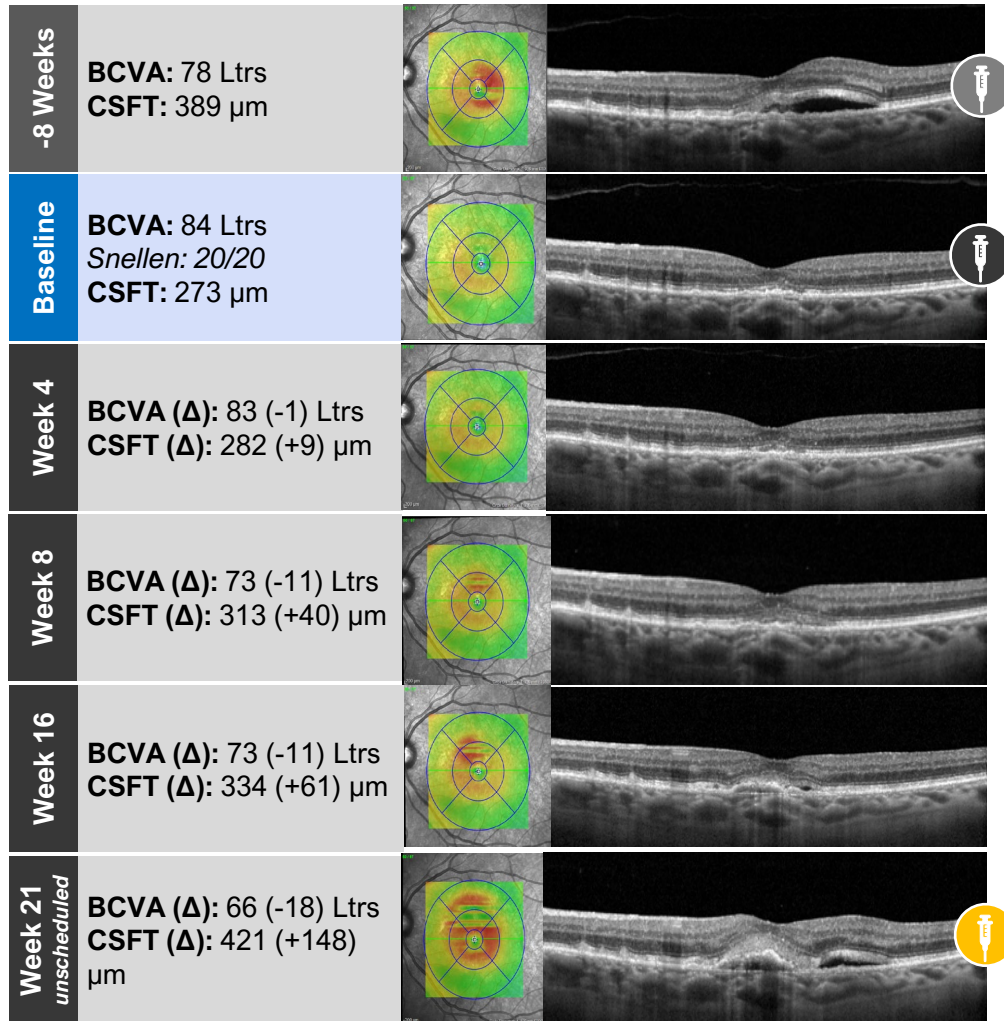
Aflibercept Case 1

 Screening
Aflibercept
(2mg)

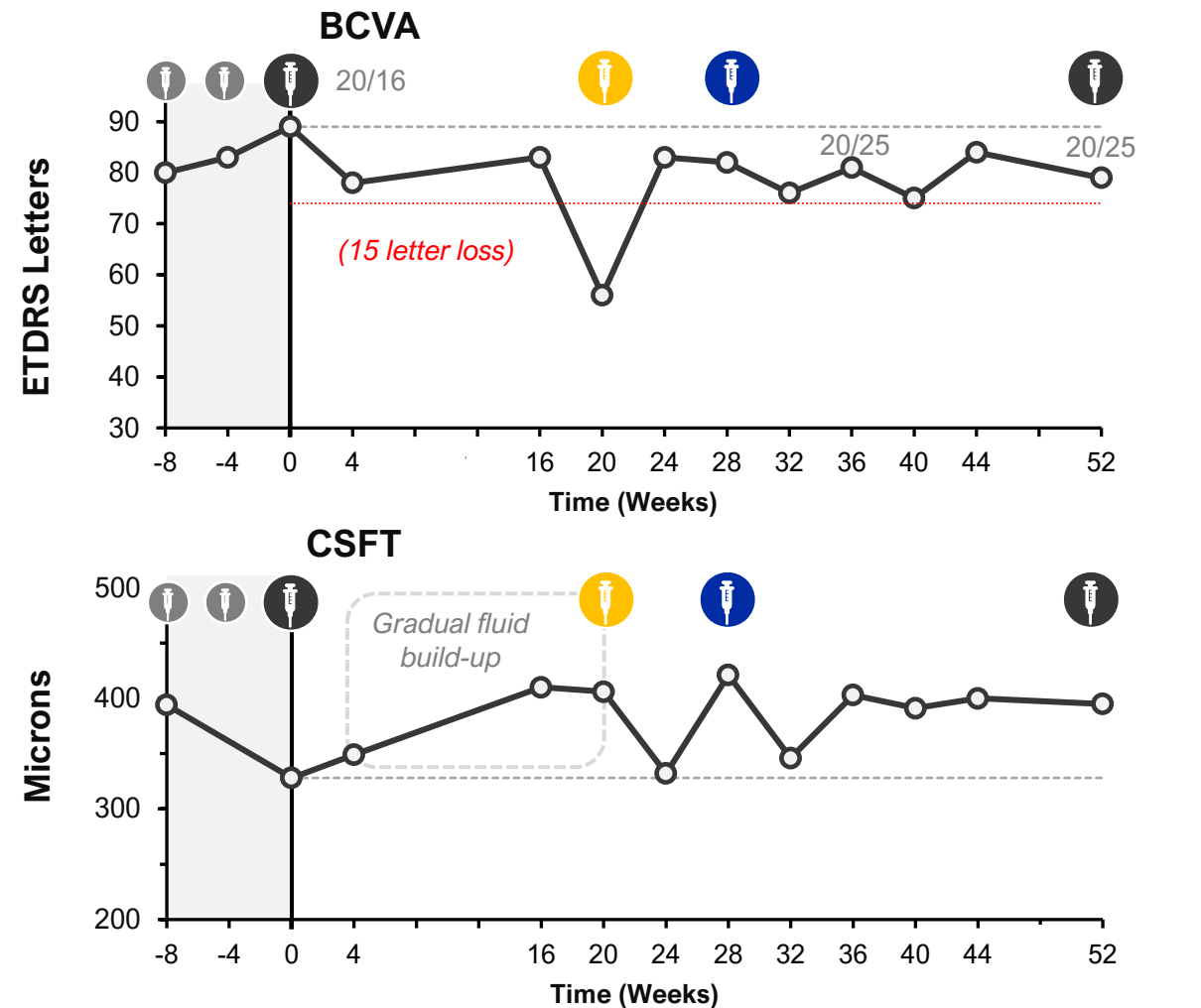
 Study
Aflibercept (2 mg)

 Per-Protocol Rescue
Aflibercept (2mg)

 Investigator
Discretion Rescue



Aflibercept Case 2



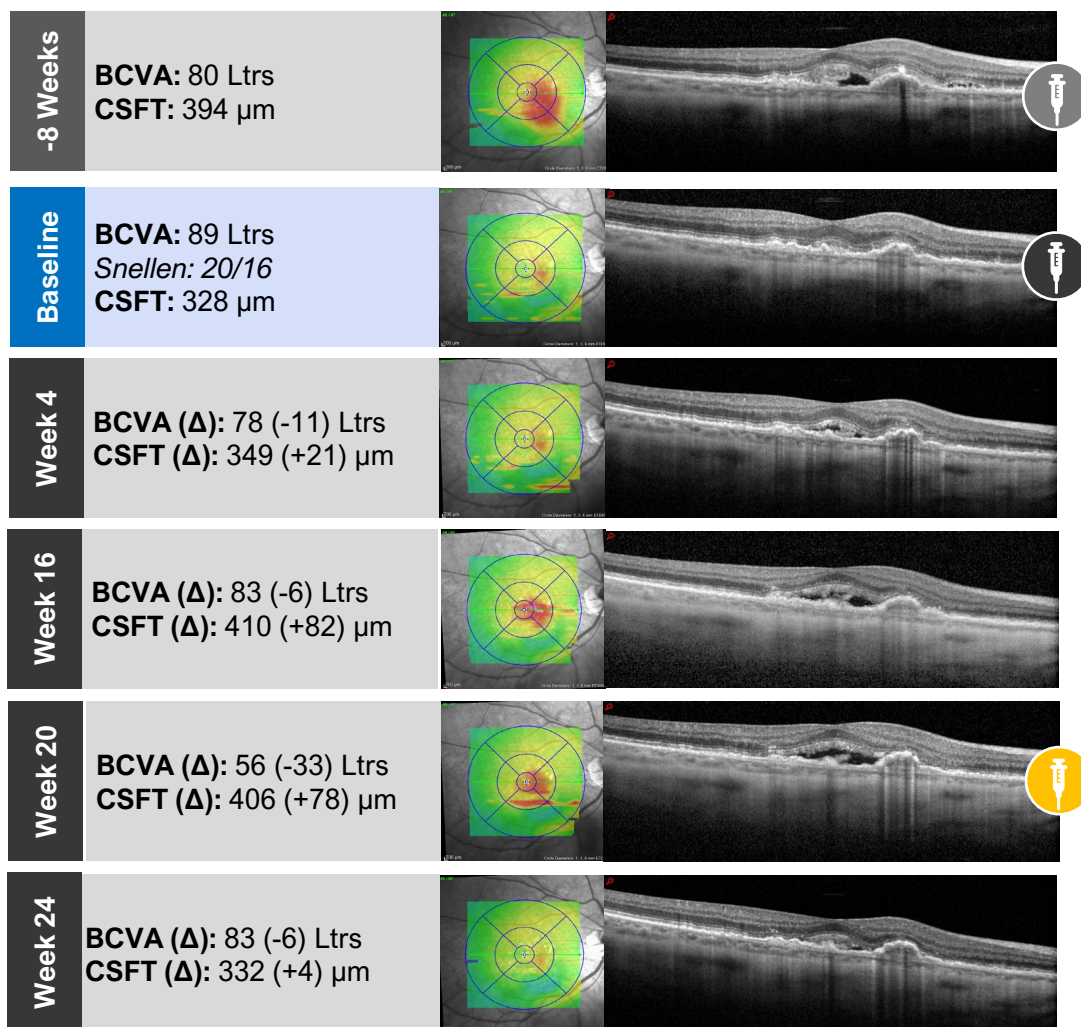
Screening Aflibercept (2mg) Study Aflibercept (2 mg) Per-Protocol Rescue Aflibercept (2mg) Investigator Discretion Rescue



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

-8 Weeks	BCVA: 80 Ltrs CSFT: 394 μ m	
Baseline	BCVA: 89 Ltrs Snellen: 20/16 CSFT: 328 μ m	
Week 4	BCVA (Δ): 78 (-11) Ltrs CSFT (Δ): 349 (+21) μ m	
Week 16	BCVA (Δ): 83 (-6) Ltrs CSFT (Δ): 410 (+82) μ m	
Week 20	BCVA (Δ): 56 (-33) Ltrs CSFT (Δ): 406 (+78) μ m	
Week 24	BCVA (Δ): 83 (-6) Ltrs CSFT (Δ): 332 (+4) μ m	
Week 28	BCVA (Δ): 82 (-7) Ltrs CSFT (Δ): 421 (+93) μ m	
Week 36	BCVA (Δ): 81(-8) Ltrs Snellen: 20/25 CSFT (Δ): 403 (+75) μ m	

Aflibercept Case 2

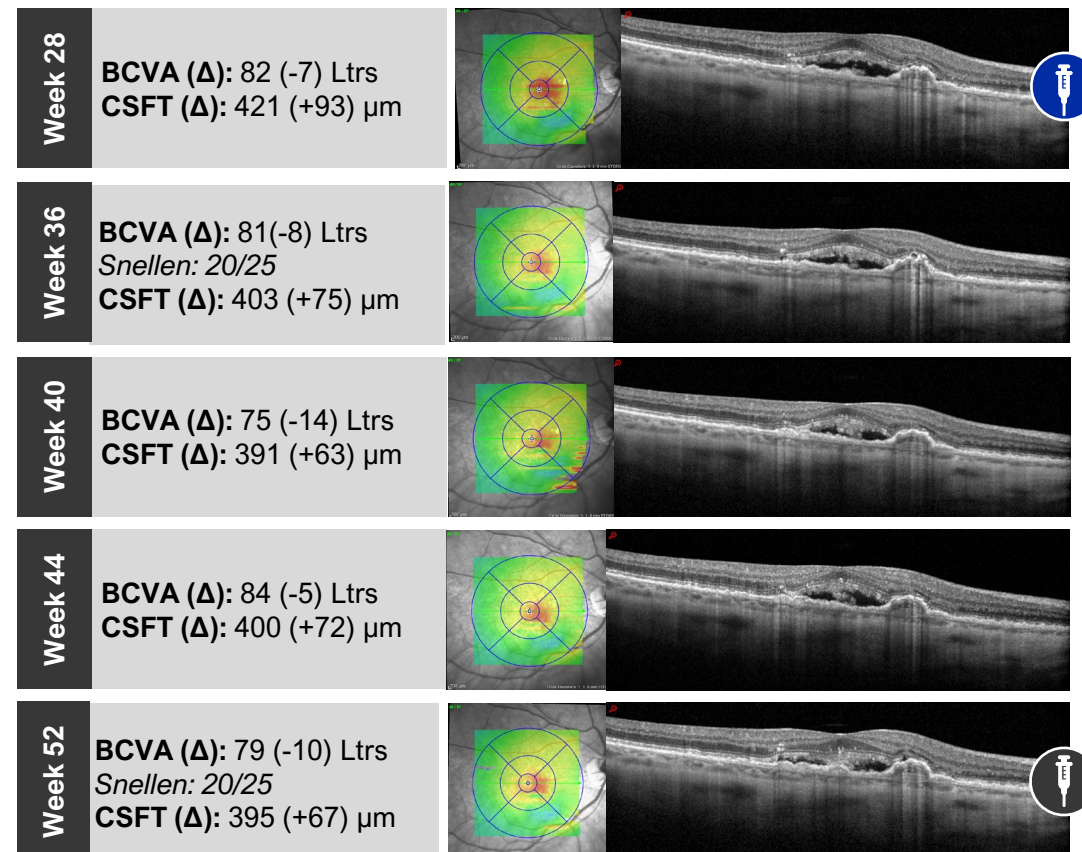


Screening Aflibercept (2mg) injection

Study Aflibercept (2 mg) administration

Per-Protocol Rescue Aflibercept (2mg)

Investigator Discretion Rescue



Discussion

Faculty



Mark R. Barakat
MD, FASRS

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



Dilsher S. Dhoot
MD, FASRS

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



Arshad M. Khanani
MD, MA, FASRS

Managing Partner, Director of
Clinical Research, Director of
Fellowship at Sierra Eye
Associates, and Clinical Associate
Professor at University of Nevada,
Reno, NV, USA

Redefining the Management of nAMD

The Impact of Durability and Sustained Disease Control

October 10, 2026

American Academy of Ophthalmology | New Orleans, LA

