

Efficacy and Safety of Intravitreal Axitinib Hydrogel (OTX-TKI) in Neovascular Age-Related Macular Degeneration

Phase 3 SOL-1 Trial Results

Patricio G. Schlottmann, MD¹

Arshad M. Khanani, MD²; Dilsher D. Dhoot, MD³; Mark R. Barakat, MD⁴; on behalf of the SOL-1 study investigators

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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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Disclosures

Patricio G. Schlottmann

- **Consultant:** Ocular Therapeutix, Novartis, Roche/Genentech, Janssen, Ora, Nanoscope, EyeBio/Merck, 4DMT, Kodiak, Oculis, Abbvie, Horizon Surgical, Adverum, Revopsis, Merit, Amgen, Kodiak
 - **Research support:** Ocular Therapeutix, 4DMT, EyeBio/Merck, Roche/Genentech, Priovant, Kodiak
-

Arshad M. Khanani

- **Consultant:** Abbvie, ADARx Pharmaceuticals, Adverum, Alcon, Alkeus, Allgenesis, Amgen, Annexin, Annexon, Apellis Pharmaceuticals, Ashvattha, Therapeutics, Astellas, Aviceda Therapeutics, Beacon Therapeutics, Boehringer Ingelheim, Clearside Biomedical, Complement Therapeutics, 4DMT, Entarada, Exegenesis, EyePoint Pharmaceuticals, Fronterra Therapeutics, Genentech, Harrow, i-Lumen Scientific, InFocus, Iveric Bio, Janssen Pharmaceuticals, Kriya Therapeutics, Kyowa Kirin, Lexitas, Merit, Neurotech, Nanoscope, Novartis, Ocugen, Ocular Therapeutix, Oculis, Ollin, Opthea, 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
 - **Research support:** Aviceda, Adverum, Alexion, Annexon, Astellas, Aviceda Therapeutics, Biojiva Complement Therapeutics, 4DMT, Eyepoint Pharmaceuticals, Exegenesis, Genentech, Gyroscope Therapeutics, Iveric Bio, Janssen, Kyowa Kirin, Ocular, Ollin, Therapeutix, Regenxbio, Roche, Sanofi, Vanotech
 - **Stock options:** Ashvattha, Aviceda Therapeutics, Oculis, Ollin, PolyPhotonix, Recens Medical, Perfuse, RevOpsis, Vial, ZipBio
 - **Board of Directors:** Oculis
-

Dilsher S. Dhoot

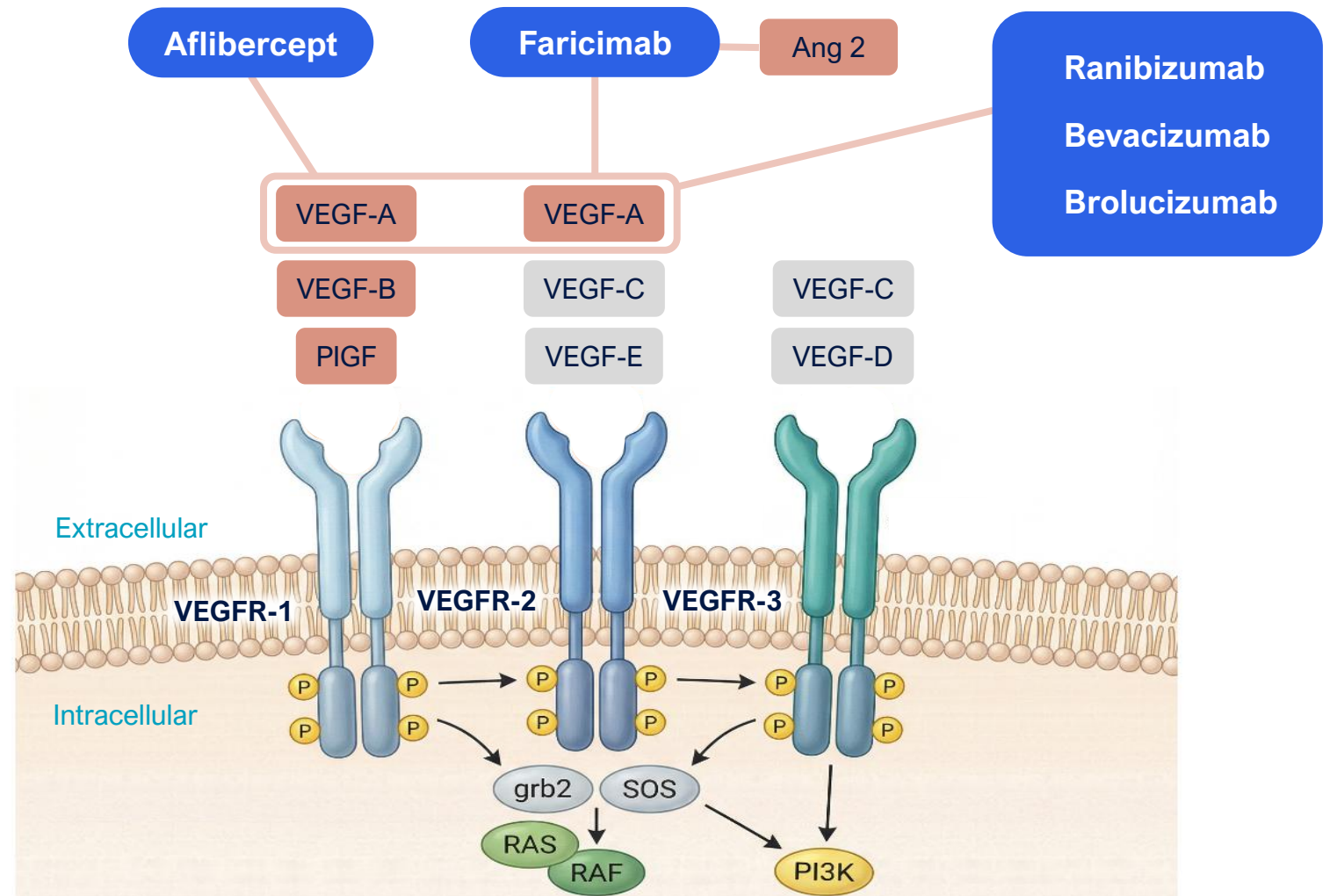
- **Consultant:** Alcon Pharmaceuticals; Alimera Sciences, Inc.; Allergan; Annexon; Apellis Pharmaceuticals, Inc.; Bayer Healthcare Pharmaceuticals, Inc.; Biocryst; Coherus; EyePoint Pharmaceuticals; Genentech; IvericBio; Novartis; Ocular Therapeutix; Optos, Inc.; Outlook Therapeutics; Oxular; Regeneron; REGENXBIO; Roche; Santen, Inc.
 - **Research Support:** Ocular Therapeutix, Inc.
-

Mark R. Barakat

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

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}

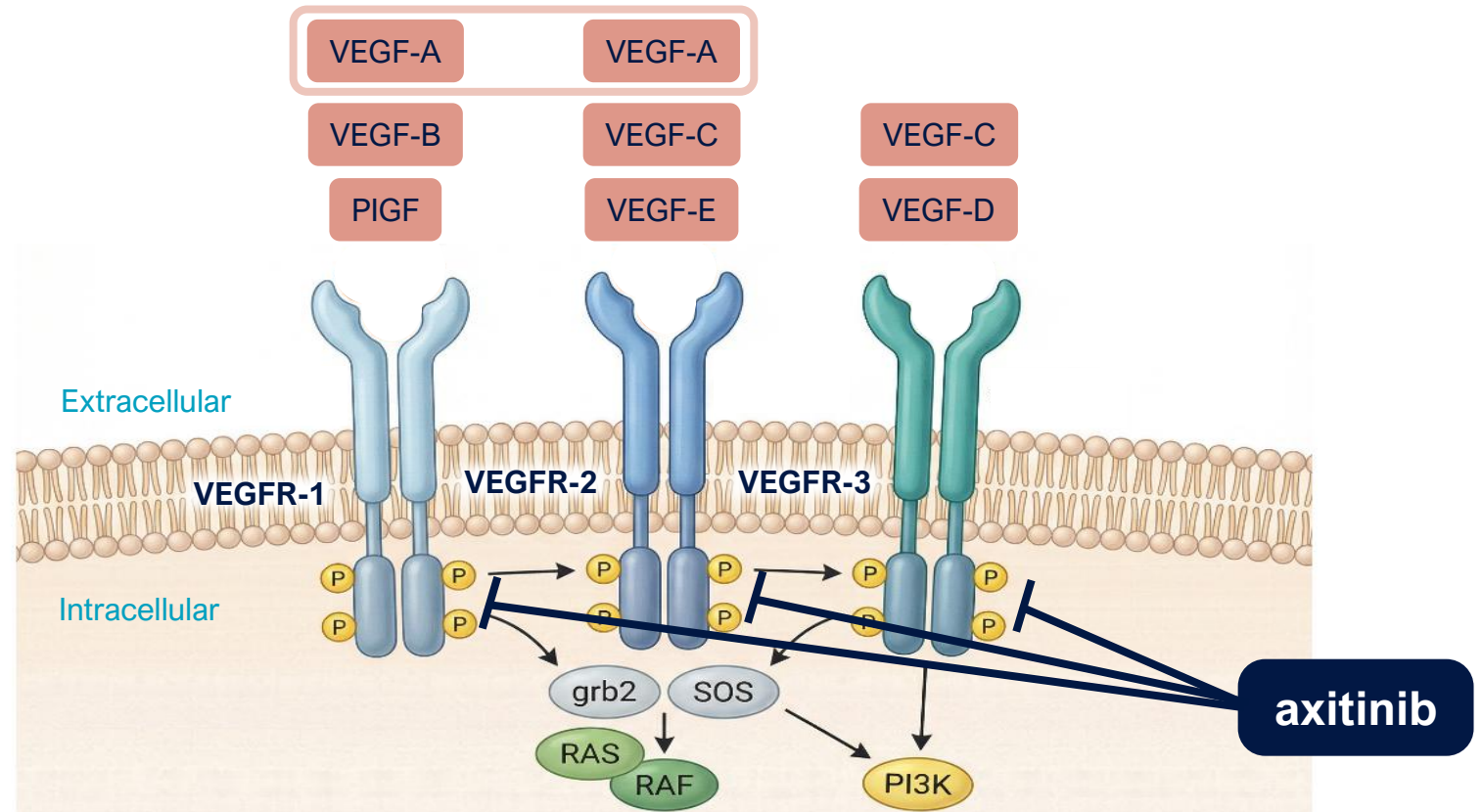


Select extracellular target binding of VEGF, PIGF and Ang-II to inhibit angiogenesis. Adapted from Zhao et al. 2015.^{2,4}

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.
 PIGF, 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}



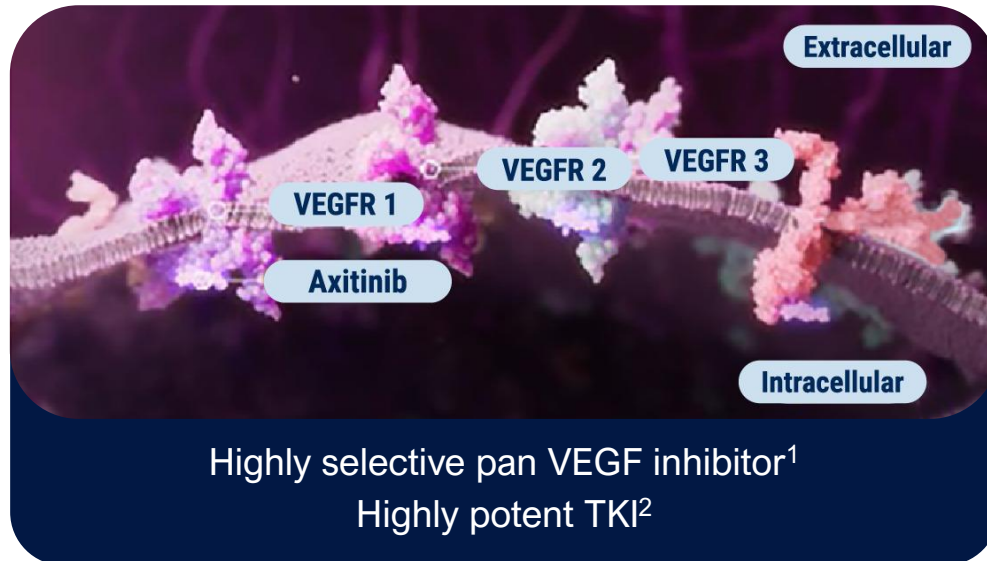
Select angiogenesis intracellular targets of inhibition for tyrosine kinase inhibitors. Adapted from Zhao et al. 2015.²⁻⁴

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. PIGF, 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

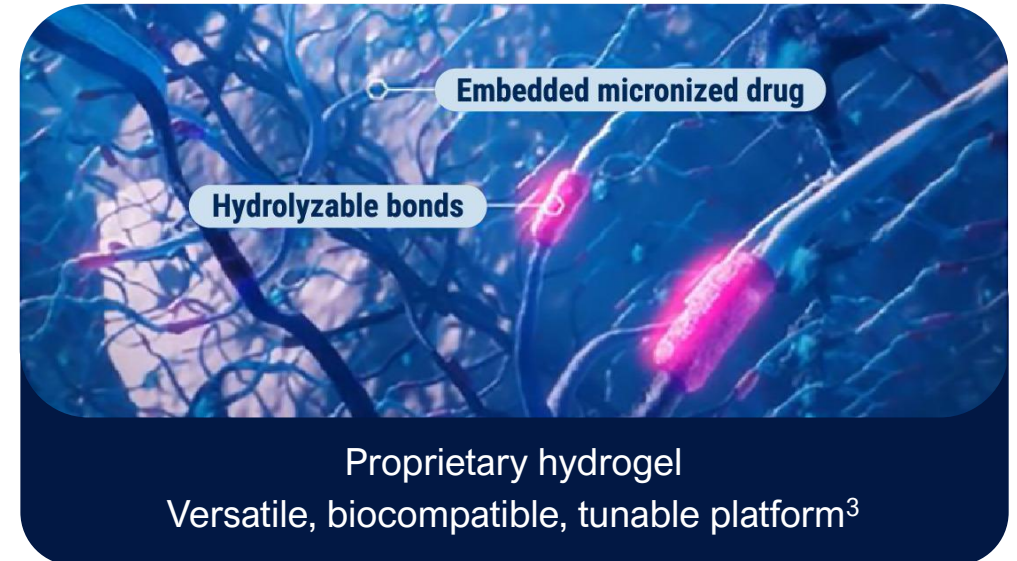
AXITINIB

Multi-target Tyrosine Kinase Inhibitor (TKI)



ELUTYX™ TECHNOLOGY

Bioresorbable, Sustained Drug Delivery



+

OTX-TKI

is being developed with the aim to provide:

A single injection,
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.

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

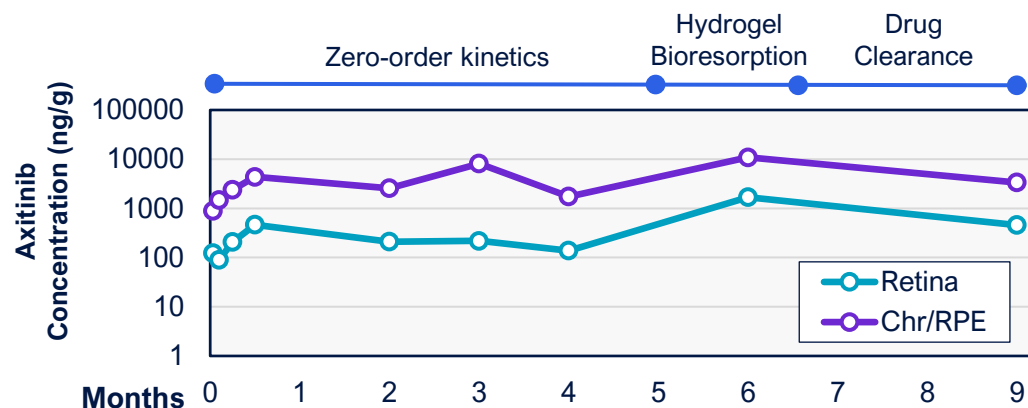
OTX-TKI is Designed to Release Axitinib and Maintain Intraocular Drug Over Time with Complete Bioresorption

OTX-TKI In Vivo Delivery Profile¹

Rapid, continuous and consistent axitinib delivery

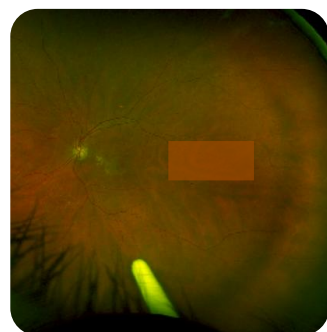
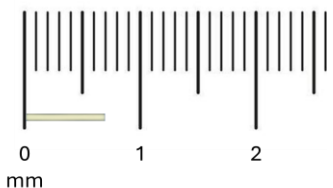
Targeted drug delivery to retina and choroid

Axitinib concentrations following a single OTX-TKI in NHPs¹

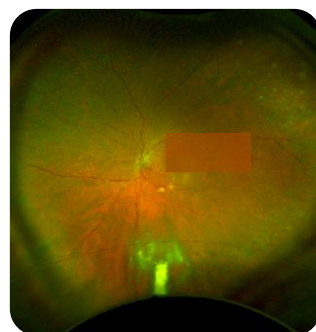


Hydrogel bioresorbs completely and predictably via hydrolysis for potential redosing¹⁻³

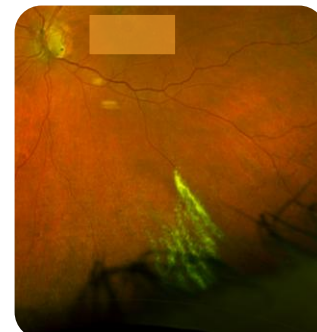
Dry OTX-TKI Dimensions
7mm length, 0.4mm diameter



Day 1



Week 20





Week 32



Week 44

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 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 |

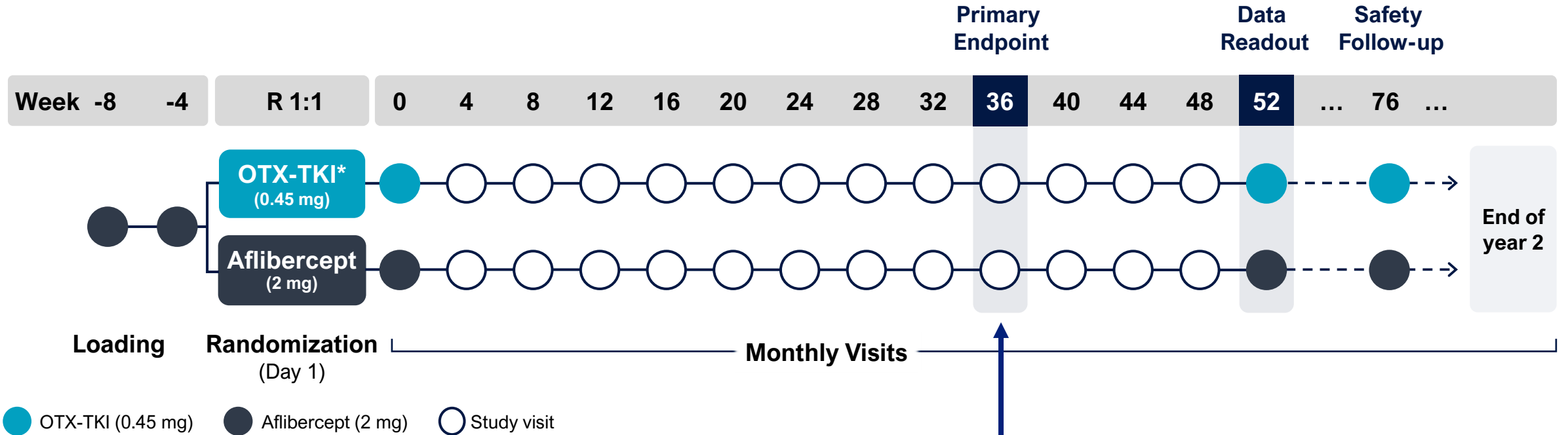


- Compares a single OTX-TKI (0.45 mg) dose to a single aflibercept (2 mg) dose
- Designed to show superiority on efficacy and durability
- SOL-1 is being conducted under a **Special Protocol Assessment**

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



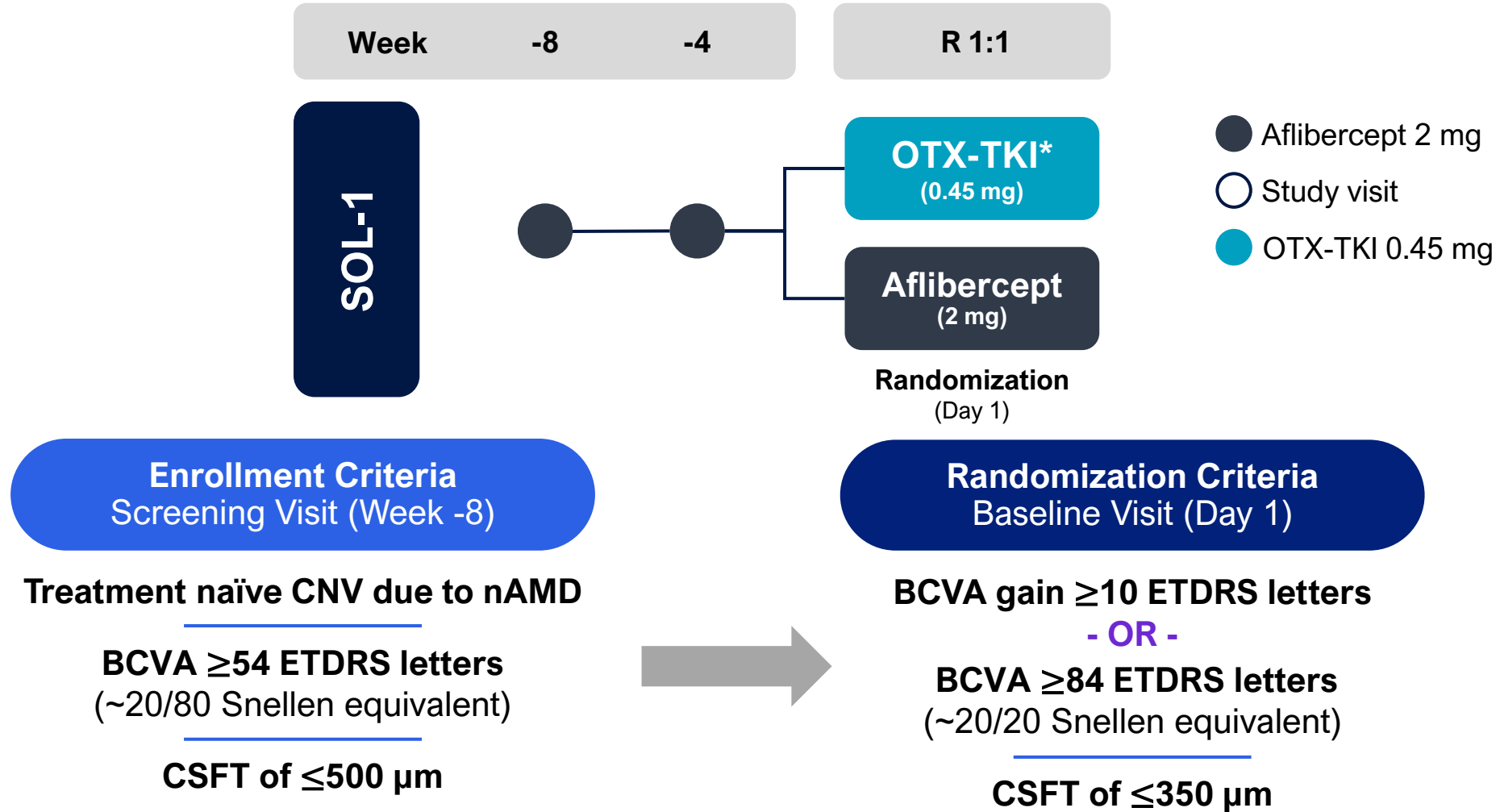
Rescue Treatment Criteria
BCVA loss ≥ 15 ETDRS letters from baseline due to nAMD
 — OR —
New macular hemorrhage that would likely lead to irreversible vision loss if left untreated in the opinion of the investigator after discussion with Medical Monitor

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

*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

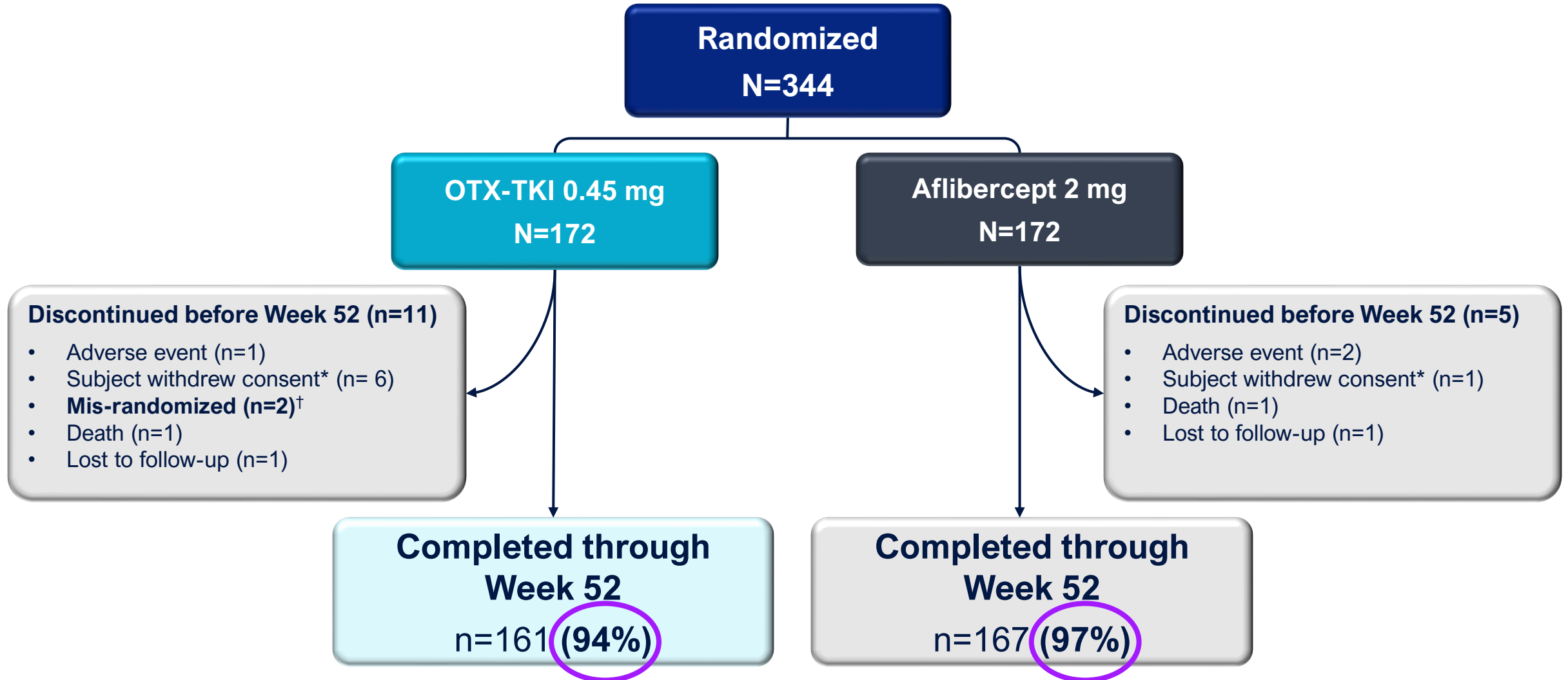


*No aflibercept injection is given at baseline
ClinicalTrials.gov. identifier: NCT06223958

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



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)

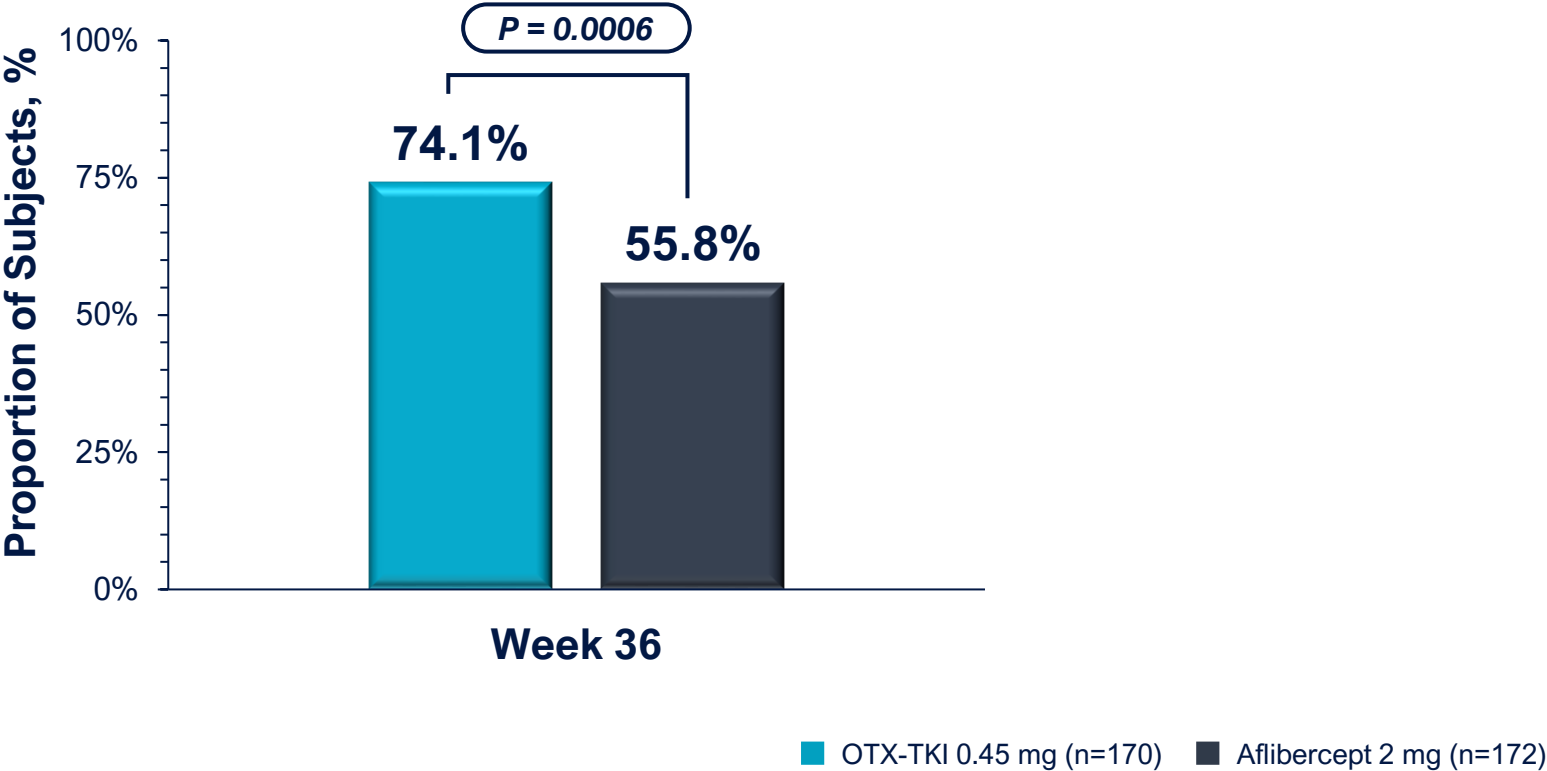
| Study Eye Characteristics | OTX-TKI 0.45 mg N = 172 | Aflibercept 2 mg N = 172 |
|---|----------------------------|-----------------------------|
| BCVA, ETDRS letter score, mean (SD) Snellen Equivalent | 70.9 (11.3) ~20/40 | 69.5 (10.8) ~20/40 |
| CSFT, μm , mean (SD) | 303.6 (72.5) | 302.7 (78.3) |

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) |

Primary Endpoint Successfully Met

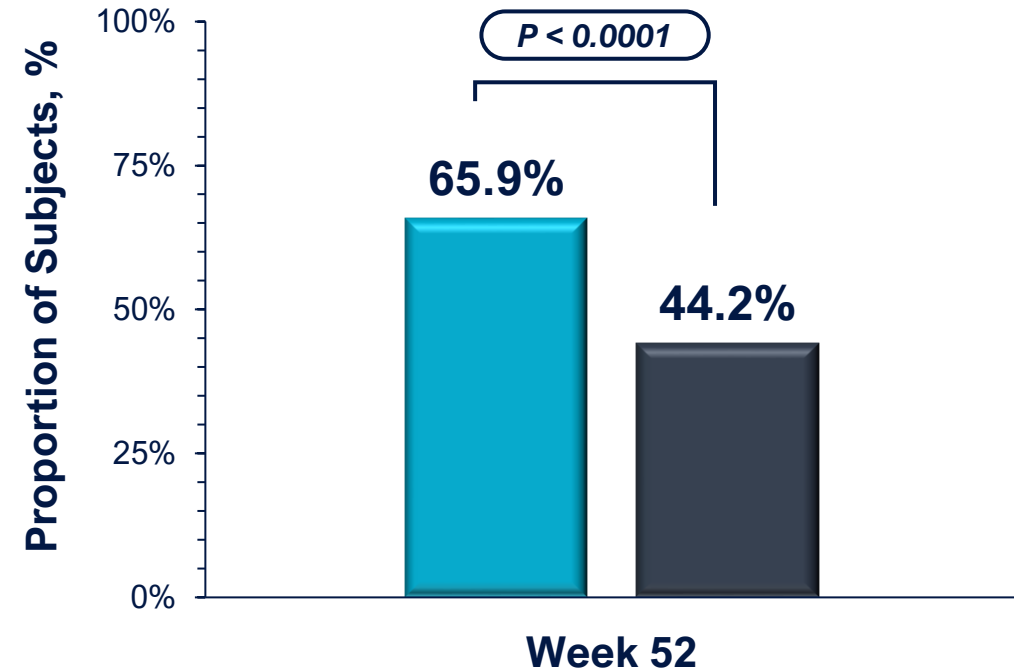
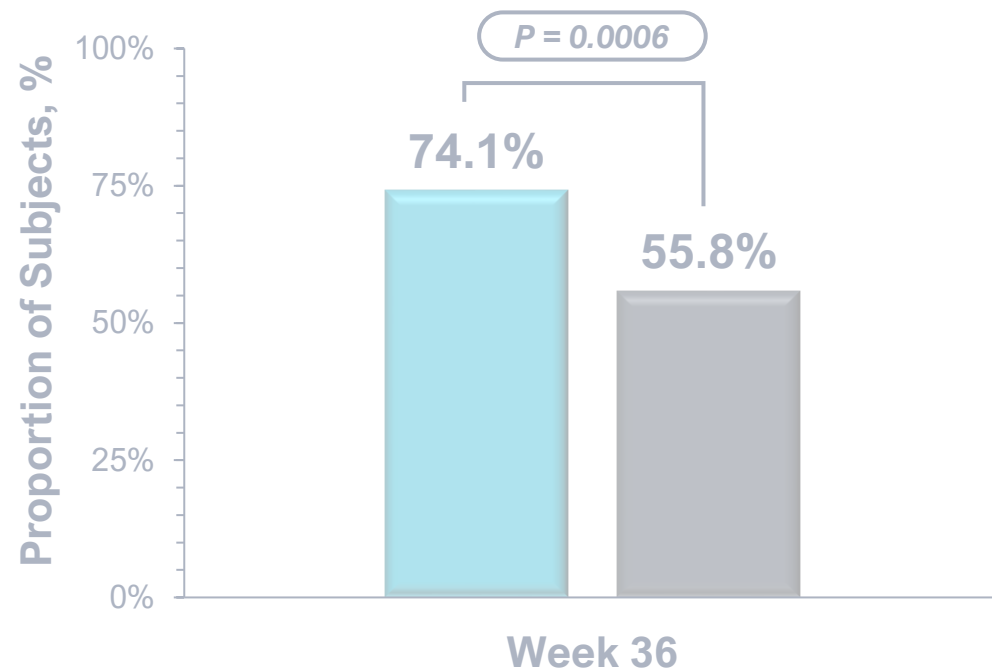
Statistically Significant Higher Proportion of Subjects Maintained Visual Acuity* with OTX-TKI vs. Aflibercept 2 mg at Week 36



*Maintenance of vision defined as proportion of subjects who maintain visual acuity, a loss of <15 ETDRS letters of BCVA from baseline
 Predefined statistical rules were applied to adjust for treatment discontinuation or deviation as per the pre-specified statistical analysis plan. Full analysis set
 BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study

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
Predefined statistical rules were applied to adjust for treatment discontinuation or deviation as per the pre-specified statistical analysis plan. Full analysis set BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study







Key Secondary and Secondary Efficacy Endpoints

Superiority Analysis per Statistical Analysis Plan

Key Secondary Endpoints

- 1 Proportion of subjects who maintained visual acuity* with one rescue injection or fewer at Week 52 
- 2 Proportion of subjects who maintained visual acuity* at Week 52 
- 3 Proportion of subjects who maintained visual acuity* with one rescue injection or fewer at Week 36 
- 4 BCVA change from baseline at Week 36 
- 5 BCVA change from baseline at Week 52 

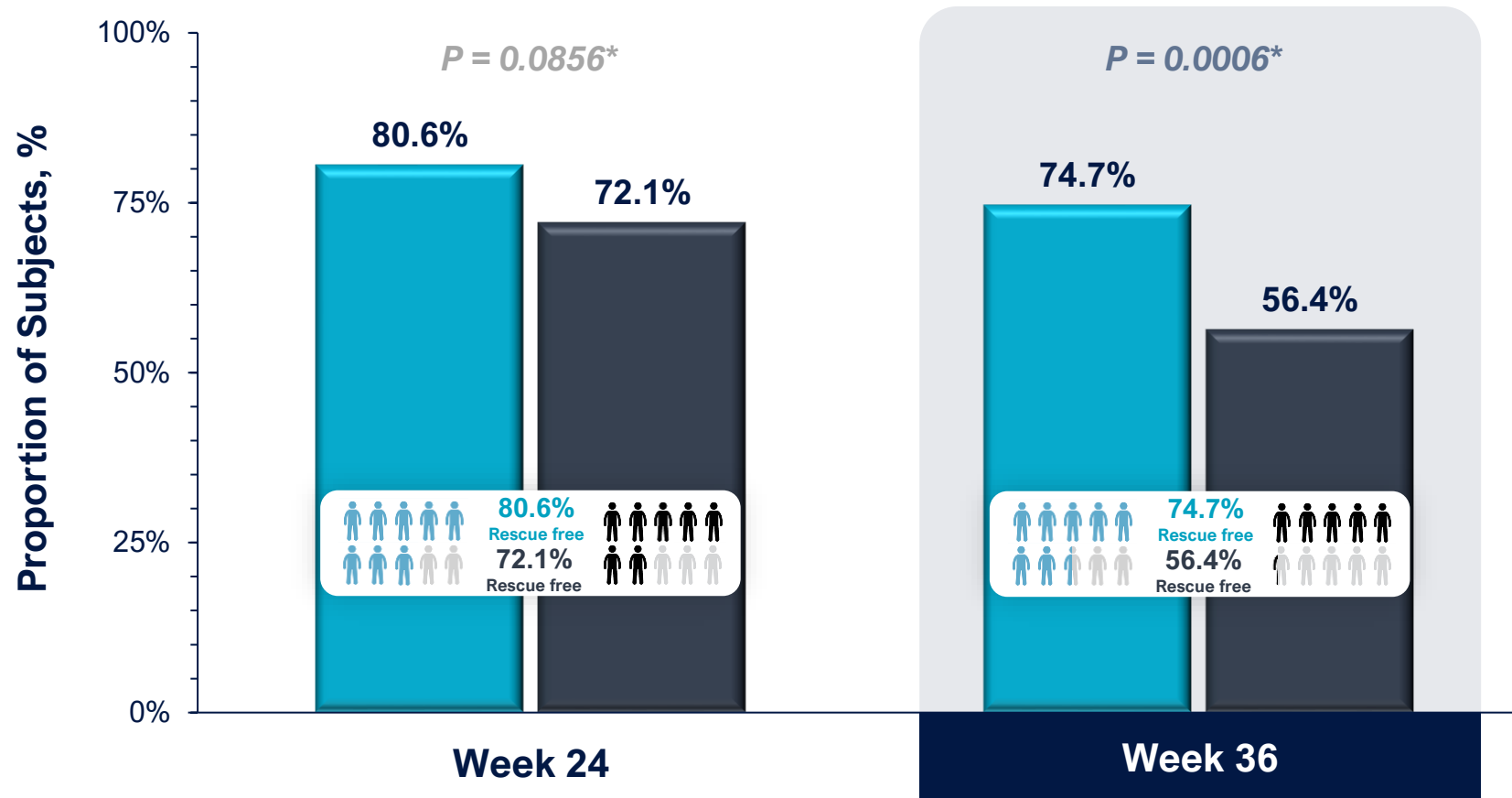
Secondary Endpoints

- 1 CSFT changes from baseline at Weeks 36 
- 2 Proportion with no CSFT increase (≤ 50 microns) at Weeks 36 
- 3 Proportion CSFT ≤ 350 microns at Weeks 36 and 52 
- 4 Mean time to the first rescue injection 
- 5 Mean time to the second rescue injection 
- 6 Proportion of subjects who lose ≥ 10 letters at Weeks 36 and 52 

*Maintained visual acuity defined as <15 ETDRS letters of BCVA loss from baseline
BCVA, Best-corrected visual acuity; CSFT Central subfield thickness

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

Proportion of Rescue-Free Subjects



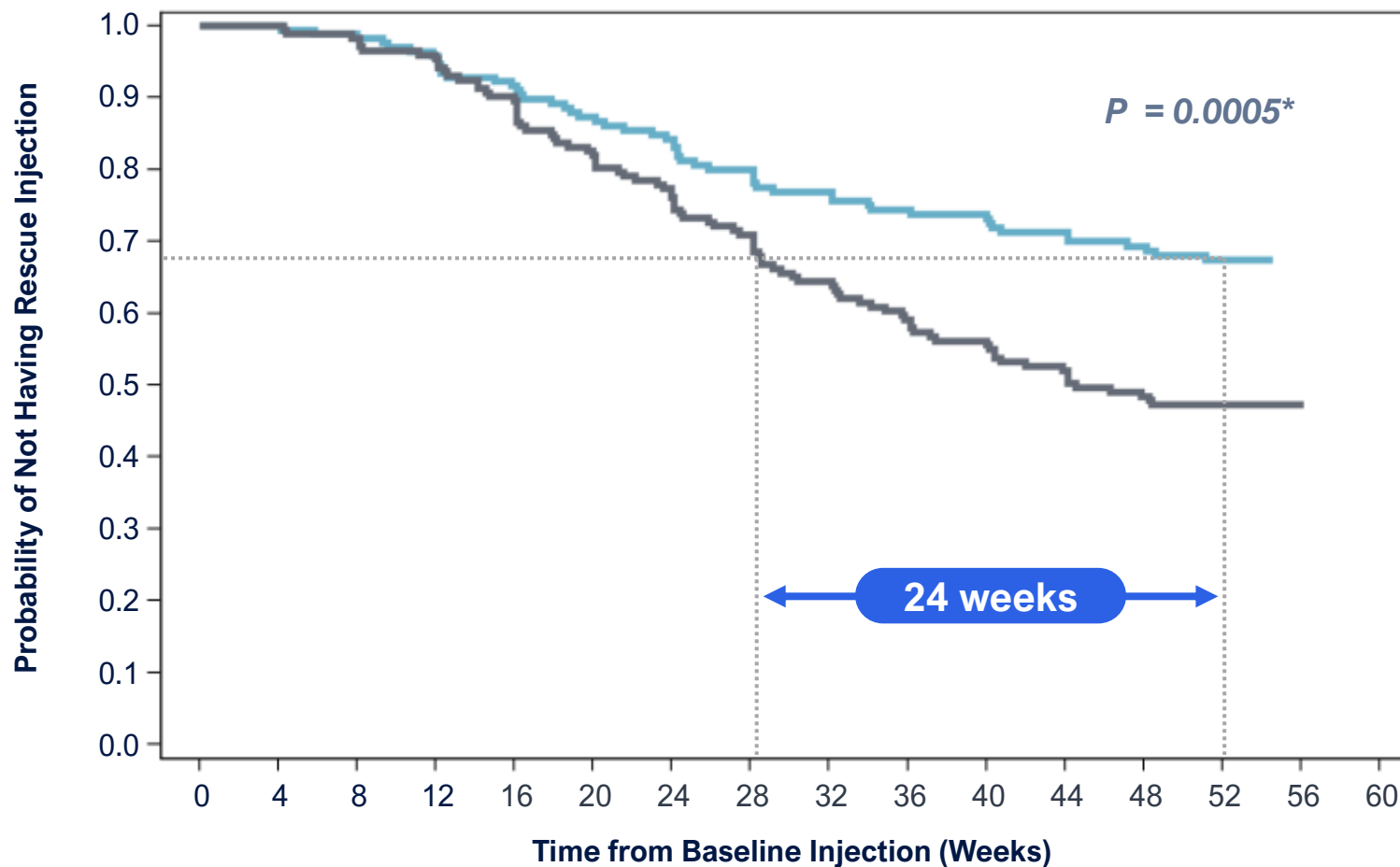
Post hoc analysis

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

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

OTX-TKI Extended Durability, Significantly Delaying First Rescue Injection

Secondary Endpoint: Time to First Rescue Treatment



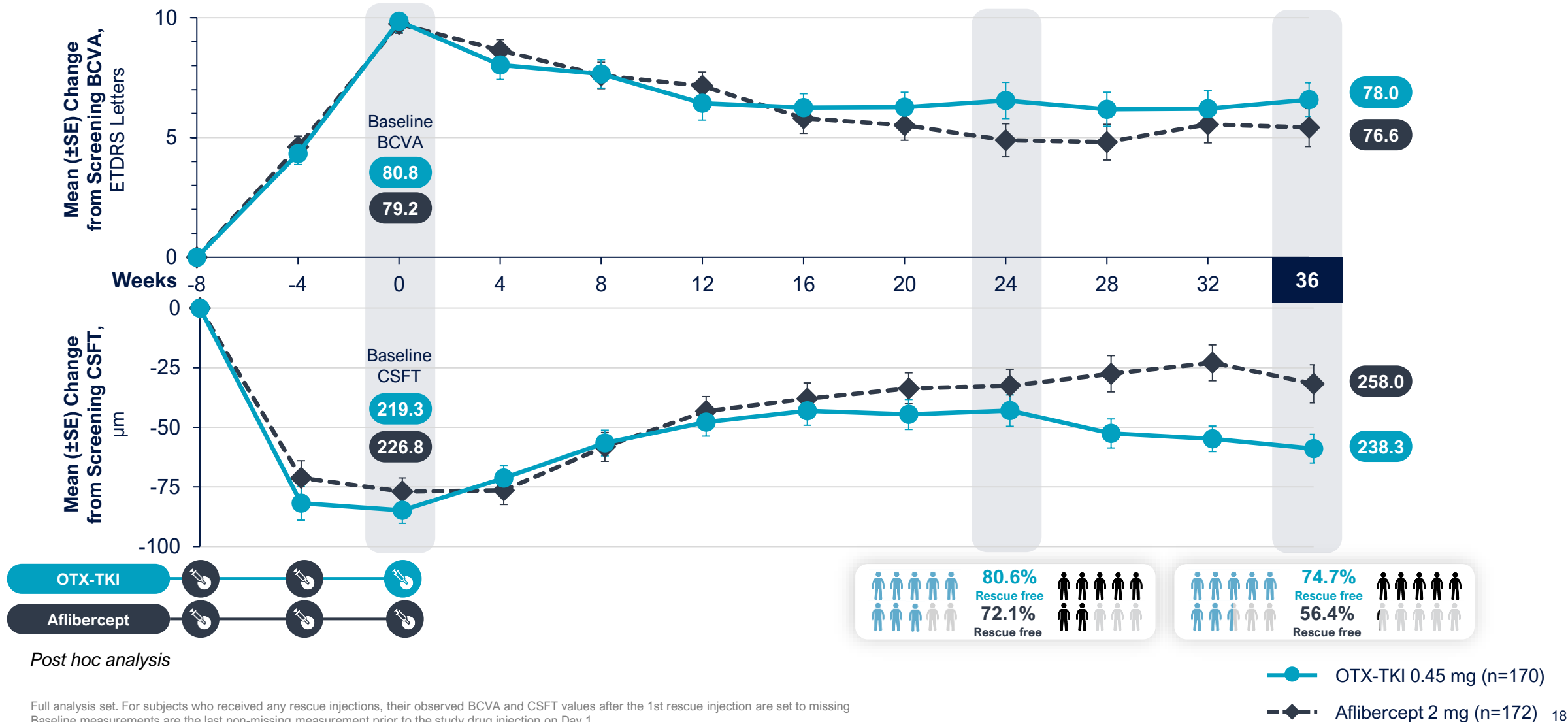
— OTX-TKI 0.45 mg (n=170)
— Aflibercept 2 mg (n=172)

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

Mean Change in BCVA and CSFT from Screening

Primary Outcome

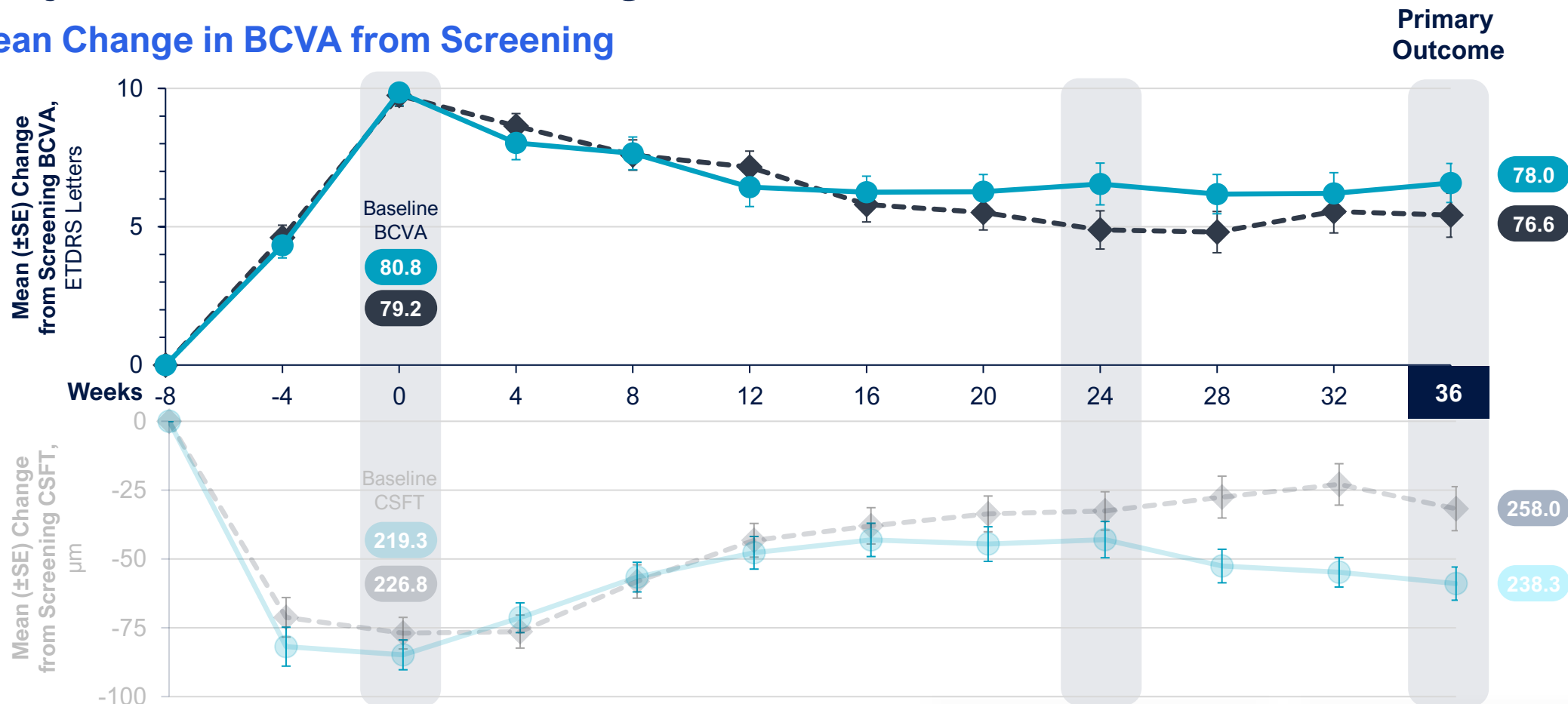


Post hoc analysis

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.

On Average, Excellent Vision at Baseline was Maintained in OTX-TKI Subjects with Most Remaining Rescue-Free

Mean Change in BCVA from Screening



OTX-TKI

Aflibercept

| | |
|-------------------------------------|-------------------------------------|
| <p>80.6% Rescue free</p> | <p>72.1% Rescue free</p> |
| <p>74.7% Rescue free</p> | <p>56.4% Rescue free</p> |

Post hoc analysis

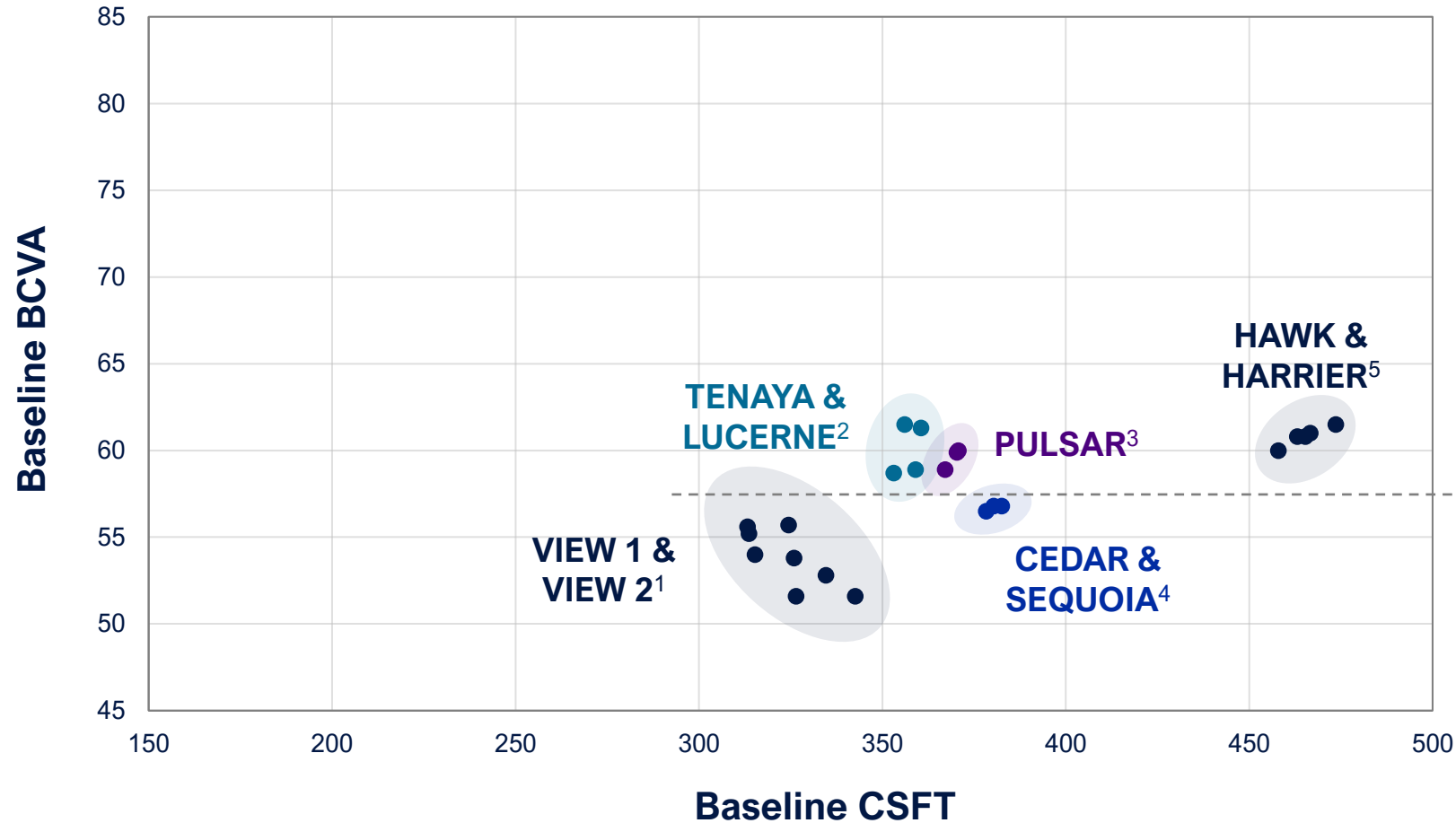
OTX-TKI 0.45 mg (n=170)
 Aflibercept 2 mg (n=172) 19

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

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



Baseline BCVA Across nAMD Trials



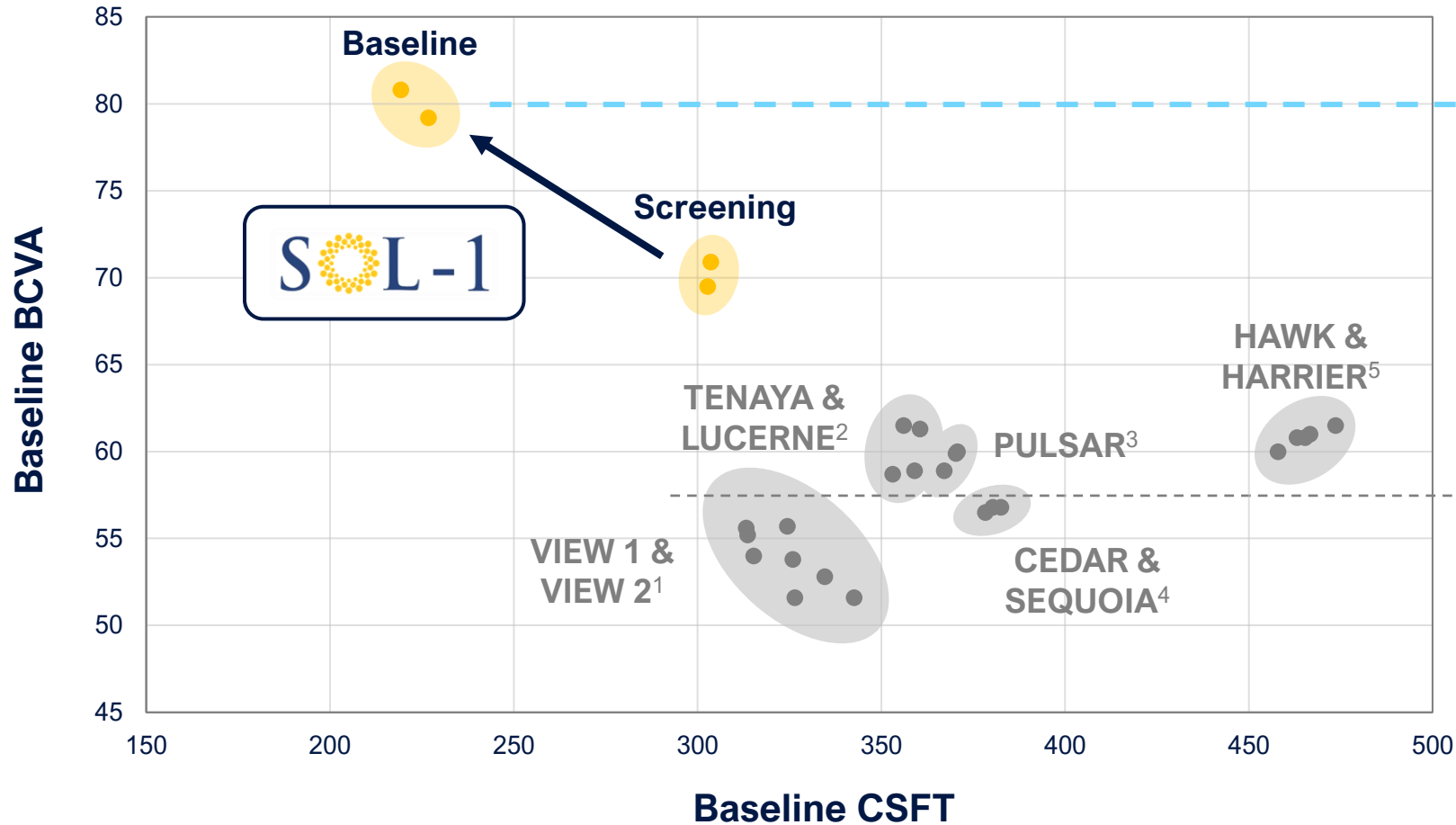
nAMD Trials
mean BCVA: 52 to 62 letters
(~20/100 to 20/60)

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 μ M**

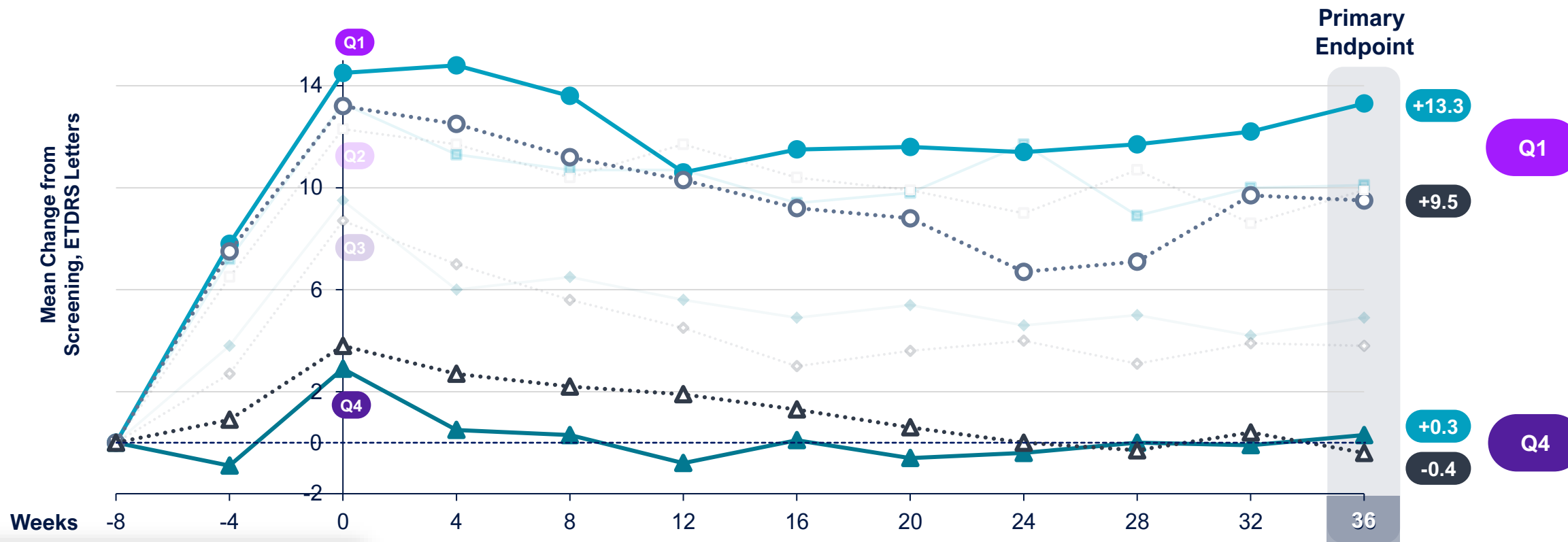
nAMD Trials

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

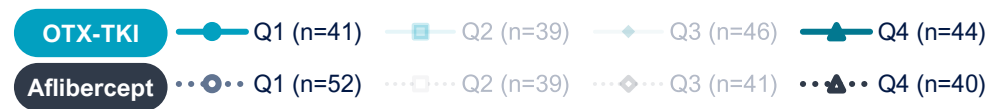
1. Heier JS, et al. *Ophthalmology*. 2012;119(12):2537-2548. 2. Heier JS, et al. *Lancet*. 2022;399(10326):729-740. 3. Lanzetta P, et al. *Lancet*. 2024;403(10432):1141-1152. 4. Kunimoto D, et al. *Ophthalmology*. 2020;127(10):1331-1344. 5. Dugel PU, et al. *Ophthalmology*. 2020;127(1):72-84.
BCVA, best-corrected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

Subjects Generally Maintained Their Initial Vision Gains

Mean Change in BCVA: By Screening BCVA



| | Mean Screening BCVA, ETDRS letters | | | |
|------------------|------------------------------------|--------|--------|--------|
| | Q1 | Q2 | Q3 | Q4 |
| OTX-TKI 0.45 mg | 55.5 | 67.2 | 75.7 | 83.6 |
| Aflibercept 2 mg | 56.8 | 66.3 | 75.7 | 82.7 |
| | ~20/80 | ~20/50 | ~20/32 | ~20/25 |

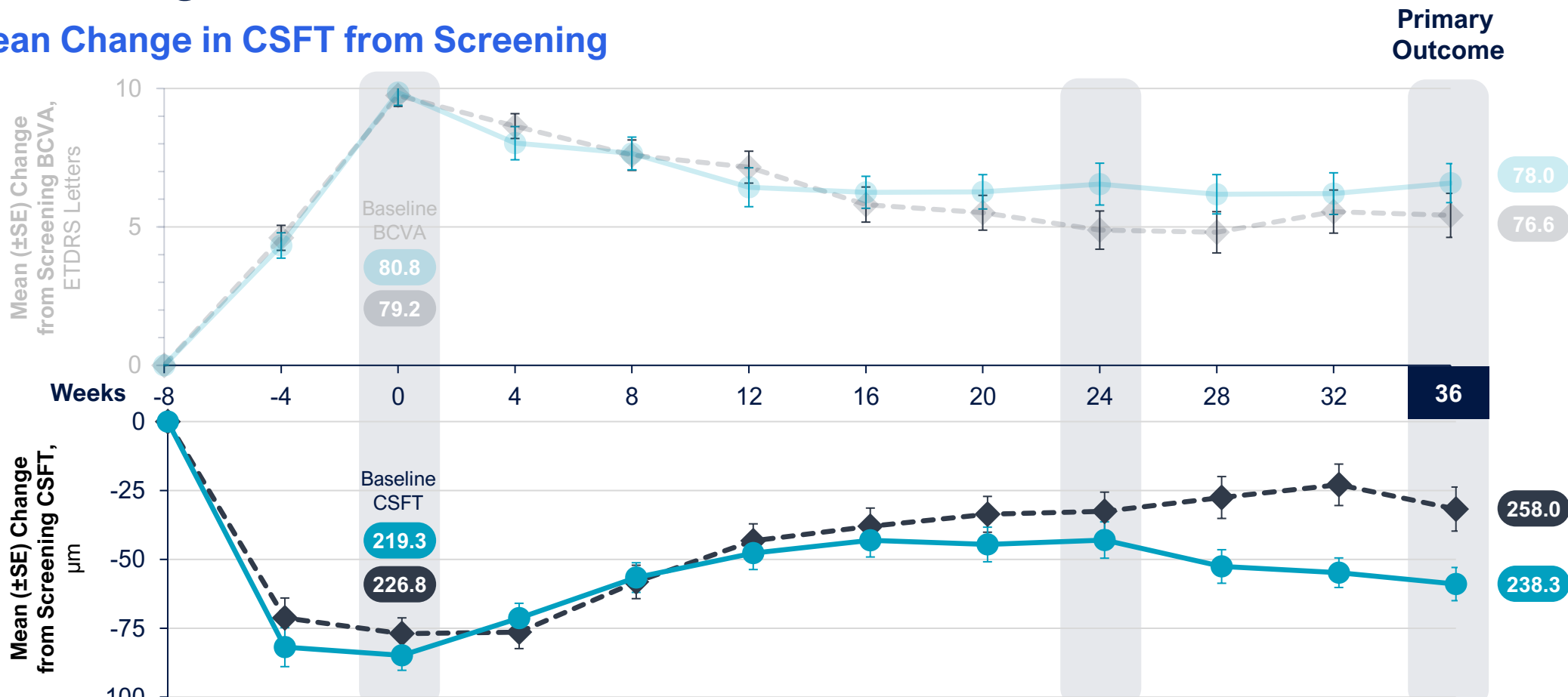


Post hoc analysis

Full analysis set
 For subjects who received any rescue injections, their observed BCVA values after the 1st rescue injection are set to missing
 BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study, Q, quartile

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

Mean Change in CSFT from Screening



OTX-TKI (n=170)

Aflibercept (n=172)

80.6% Rescue free (OTX-TKI)

74.7% Rescue free (Aflibercept)

72.1% Rescue free (OTX-TKI)

56.4% Rescue free (Aflibercept)

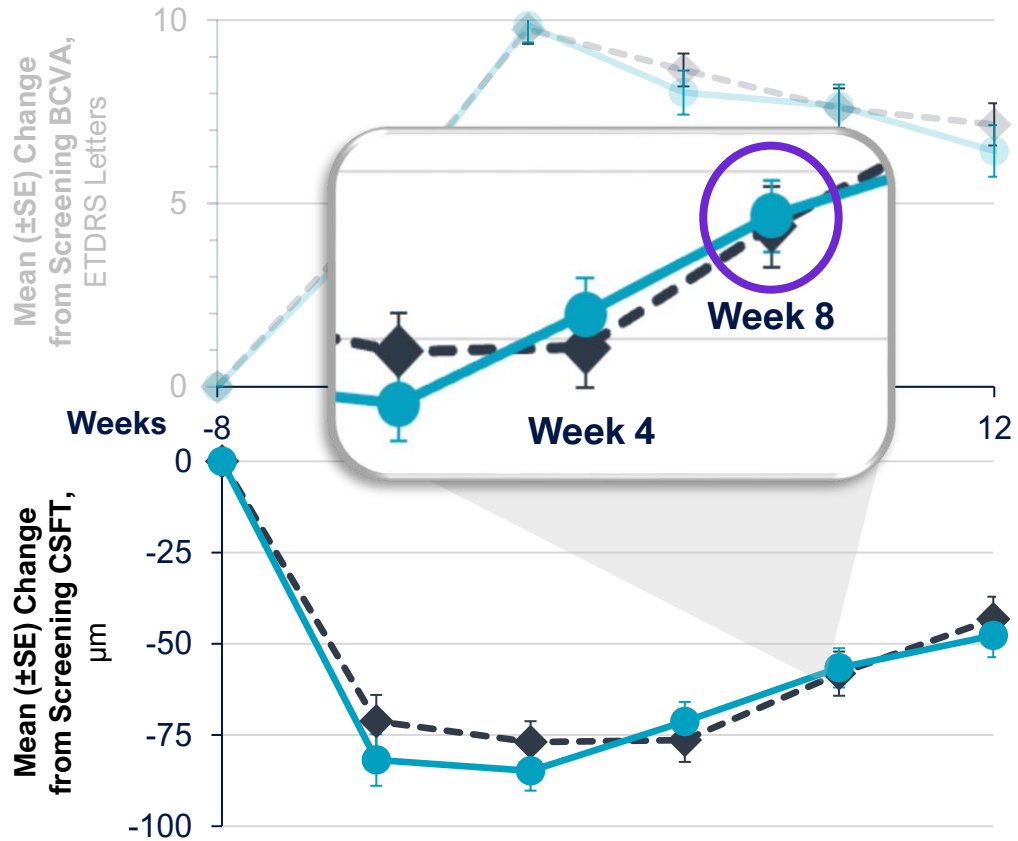
Post hoc analysis

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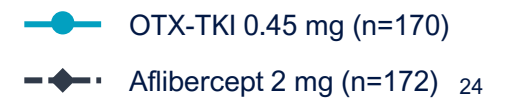
OTX-TKI 0.45 mg (n=170)
 Aflibercept 2 mg (n=172) 23

Week 8: Similar Outcomes in Both Groups

Mean Change in CSFT from Screening



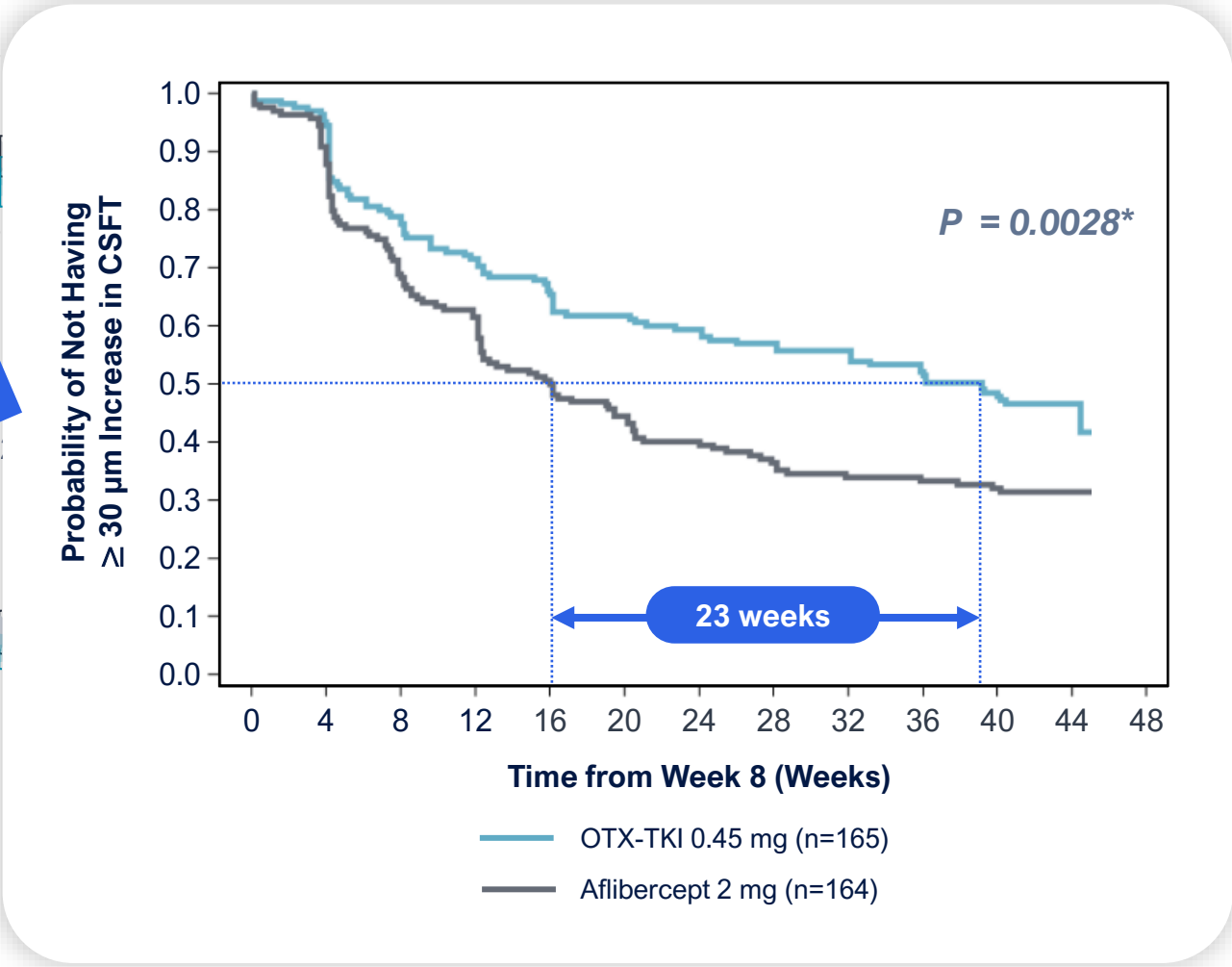
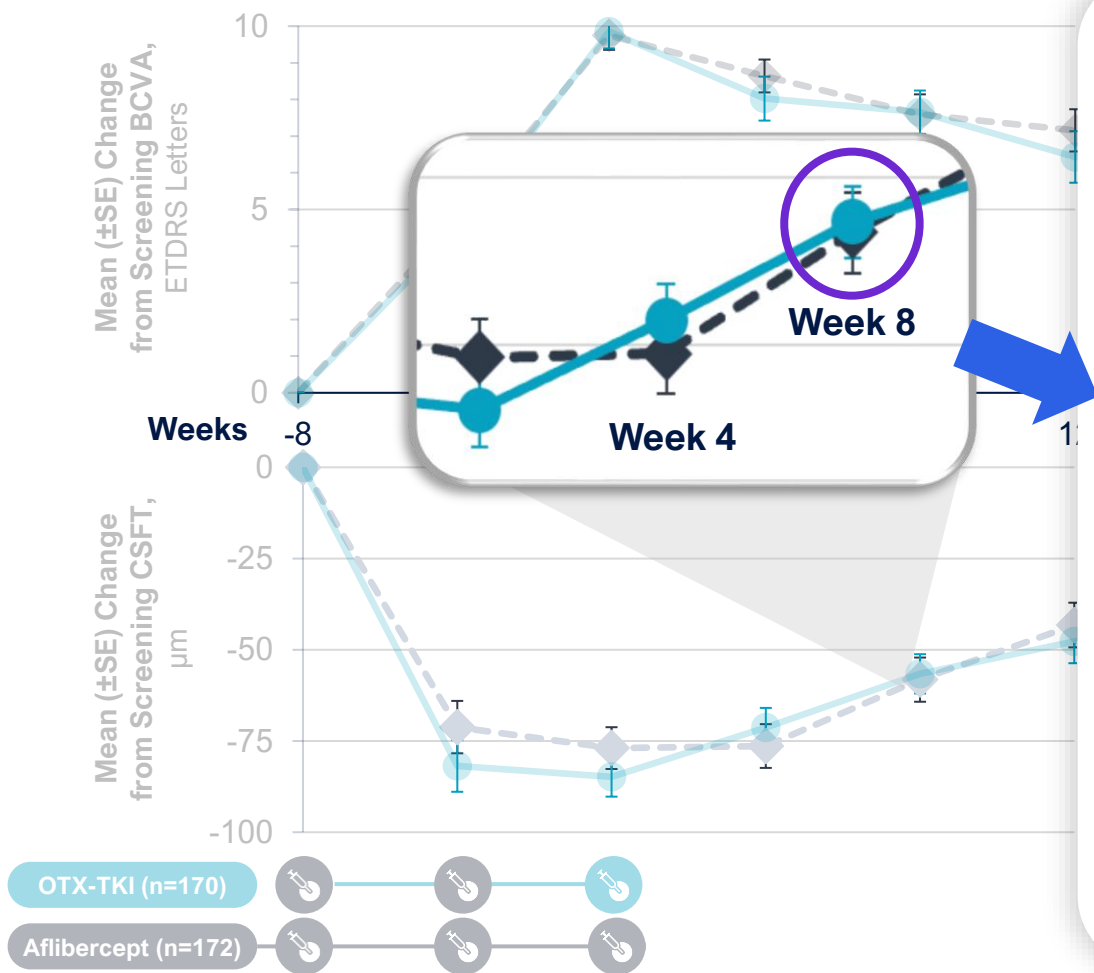
Post hoc analysis



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

Anatomic Control in Subjects Treated with OTX-TKI

Time to $\geq 30 \mu\text{m}$ Increase in CSFT from Week 8

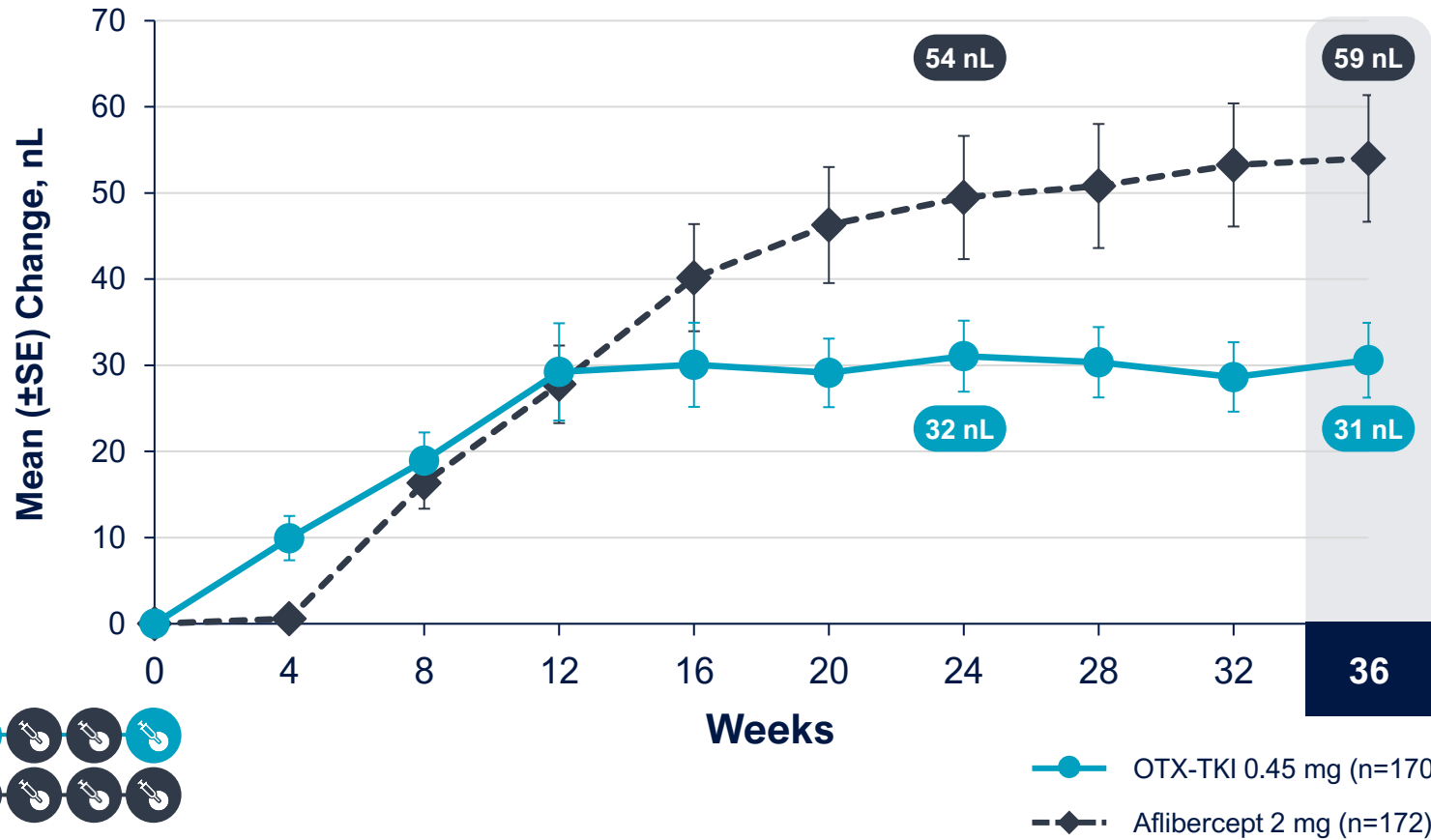


Post hoc analysis

Subjects with CSFT at Week 8 in Full Analysis Set; *Descriptive p-value CSFT; central subfield thickness, measured from the internal limiting membrane to the retinal pigment epithelium;

OTX-TKI Delivered Sustained Fluid Control

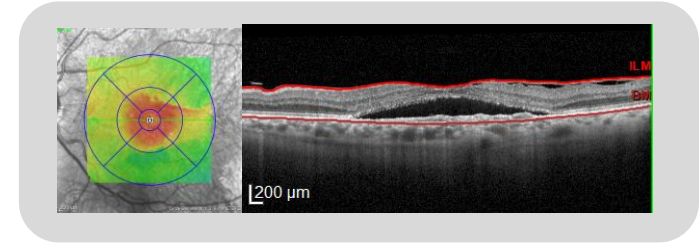
Mean Change in Intra-Retinal and Sub-Retinal Fluid Volume



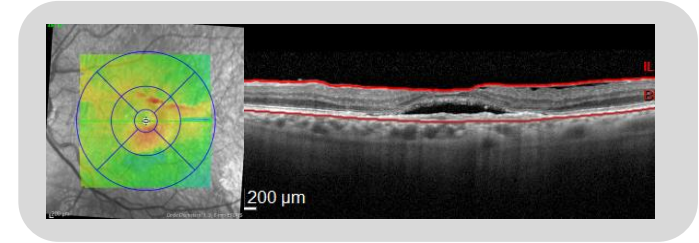
OTX-TKI

Aflibercept

Total Fluid Volume: 60 nL



Total Fluid Volume: 30 nL



Pre-specified exploratory analysis

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**

OTX-TKI was Generally Well Tolerated

Ocular Adverse Events in the Study Eye

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| 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) |

- All cases were mild to moderate in severity
- No evidence of associated IOI
- Onset 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

Superiority Primary Endpoint Successfully Met

First trial to demonstrate durability \geq 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

Thank You!