

SOL-1 Phase 3 Superiority Trial Evaluating Intravitreal Axitinib Hydrogel (OTX-TKI) in Neovascular Age-related Macular Degeneration

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Disclosures and Disclaimer

Financial Disclosures (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
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- **Speaker:** Alcon, ANI Pharmaceuticals, Apellis, Astellas, Genentech, Regeneron,
- **Stock/Stock Options:** NeuBase, Oxurion, RevOpsisTherapeutics

Investigational Product Disclosure

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

Study Design: OTX-TKI and Aflibercept Direct Comparison

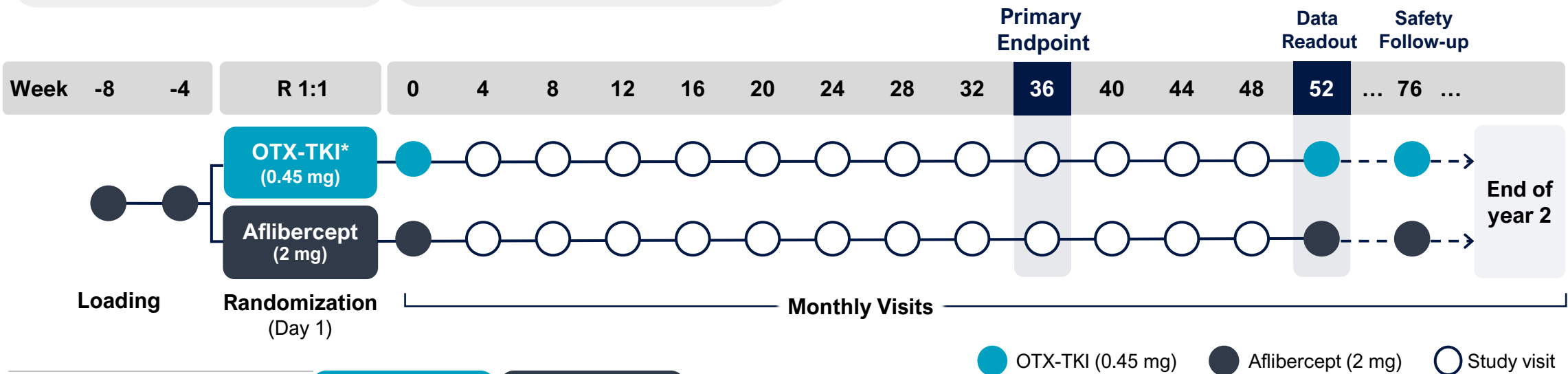
Key Enrollment Criteria (Screening)

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

Key Randomization Criteria (Day 1)

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

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



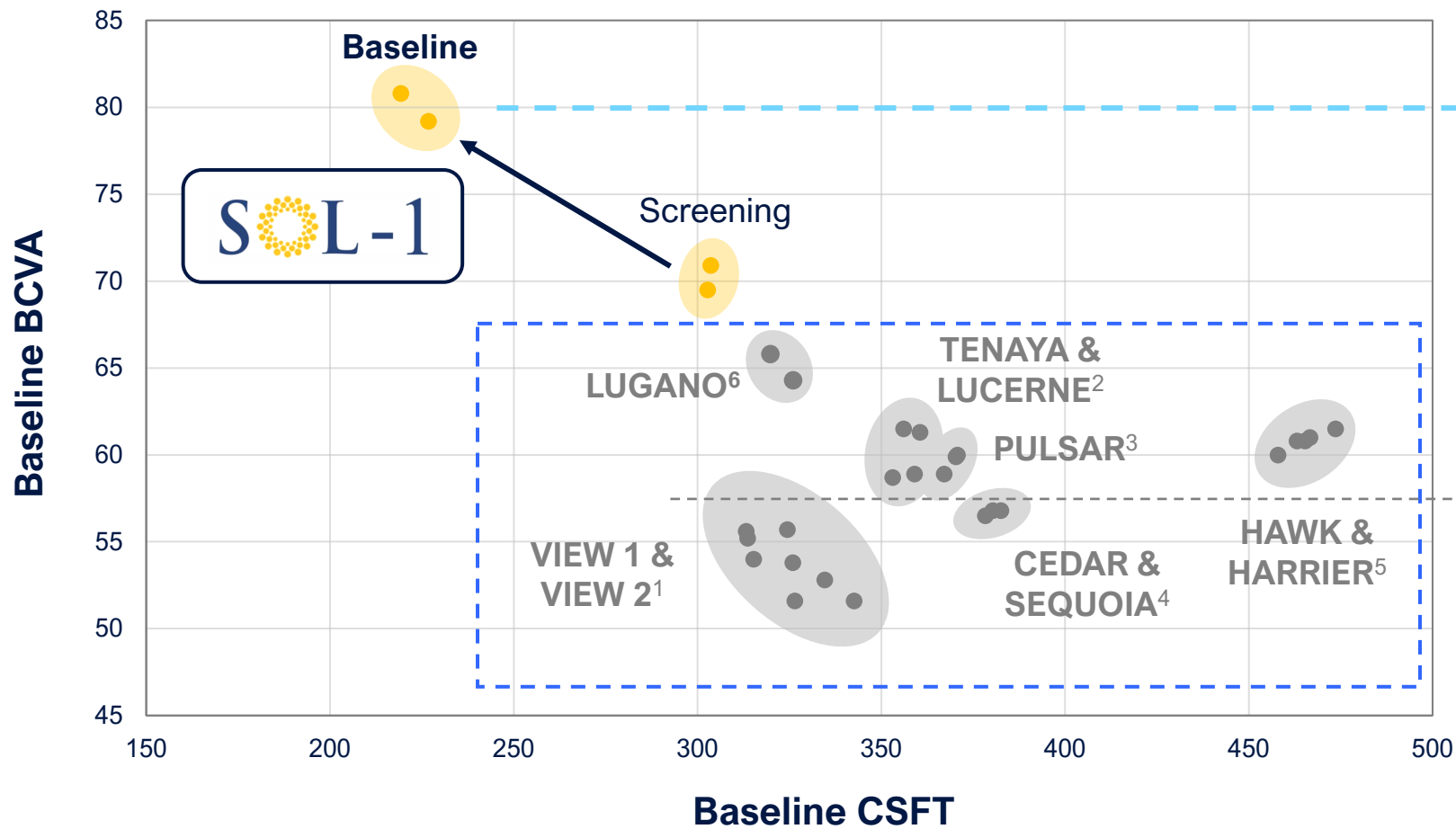
Baseline (Randomization) Study Eye Characteristics	OTX-TKI 0.45 mg N = 172 [†]	Aflibercept 2 mg N = 172
Mean (SD) BCVA, ETDRS letter score, Snellen Equivalent	80.8 (7.6) ~20/25	79.2 (7.9) ~20/25
Mean (SD) CSFT, μm ,	219.3 (37.1)	226.8 (42.1)

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

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

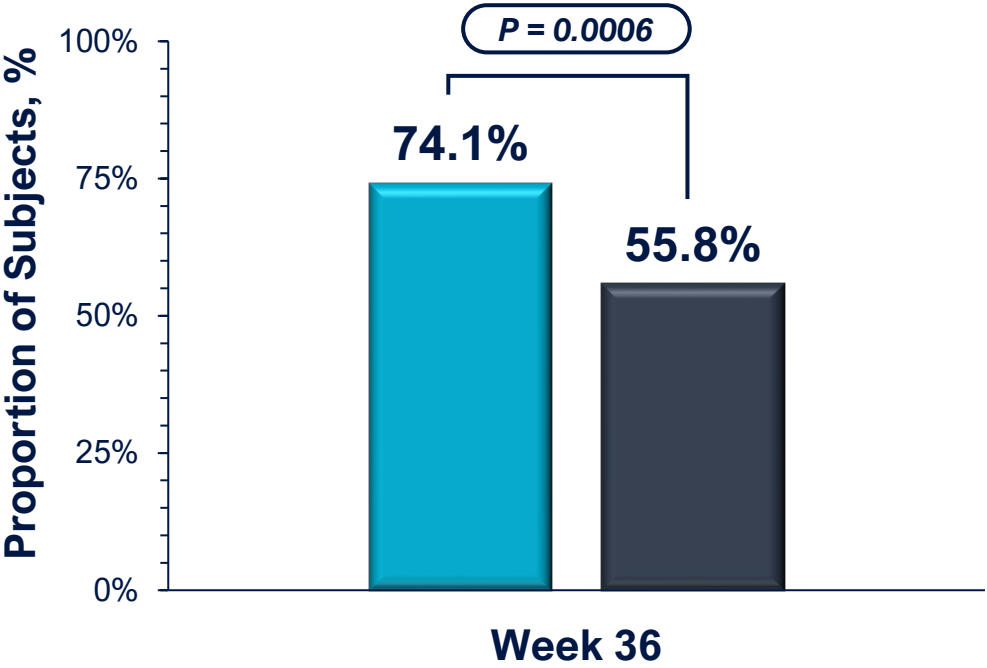
mean BCVA: **52 to 66 letters (~20/100 to 20/50)**

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. 6. Regillo CD, et al. Presented at: Retina Society Annual Meeting; September 23-26, 2026; Los Angeles, CA.

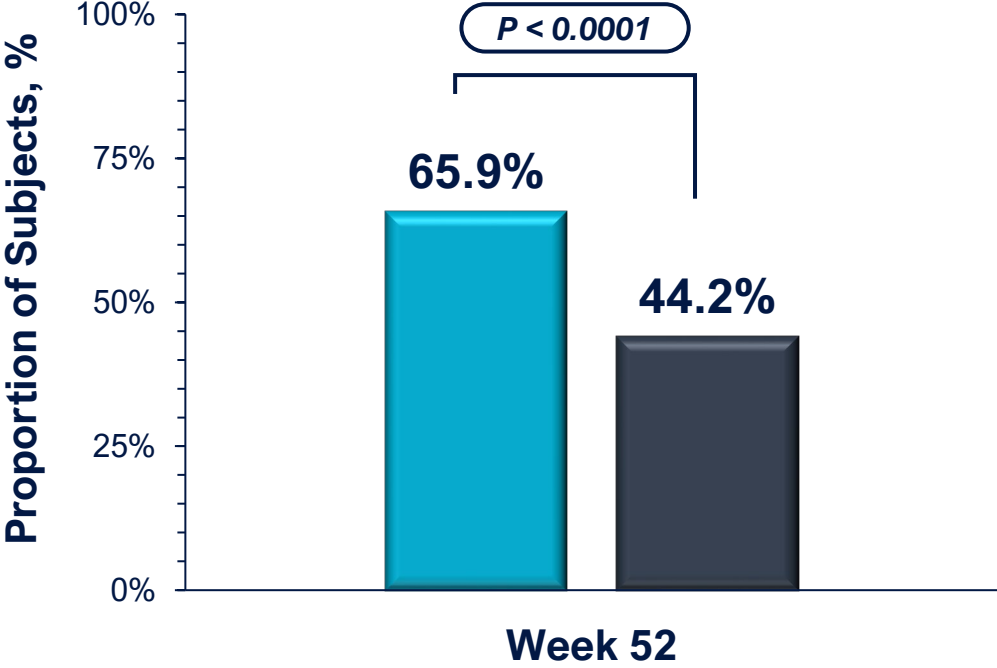
Unmatched Durability: First Trial to Demonstrate Durability ≥ 9 Months

Maintenance of Visual Acuity*

Primary Endpoint



Key Secondary Endpoint



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

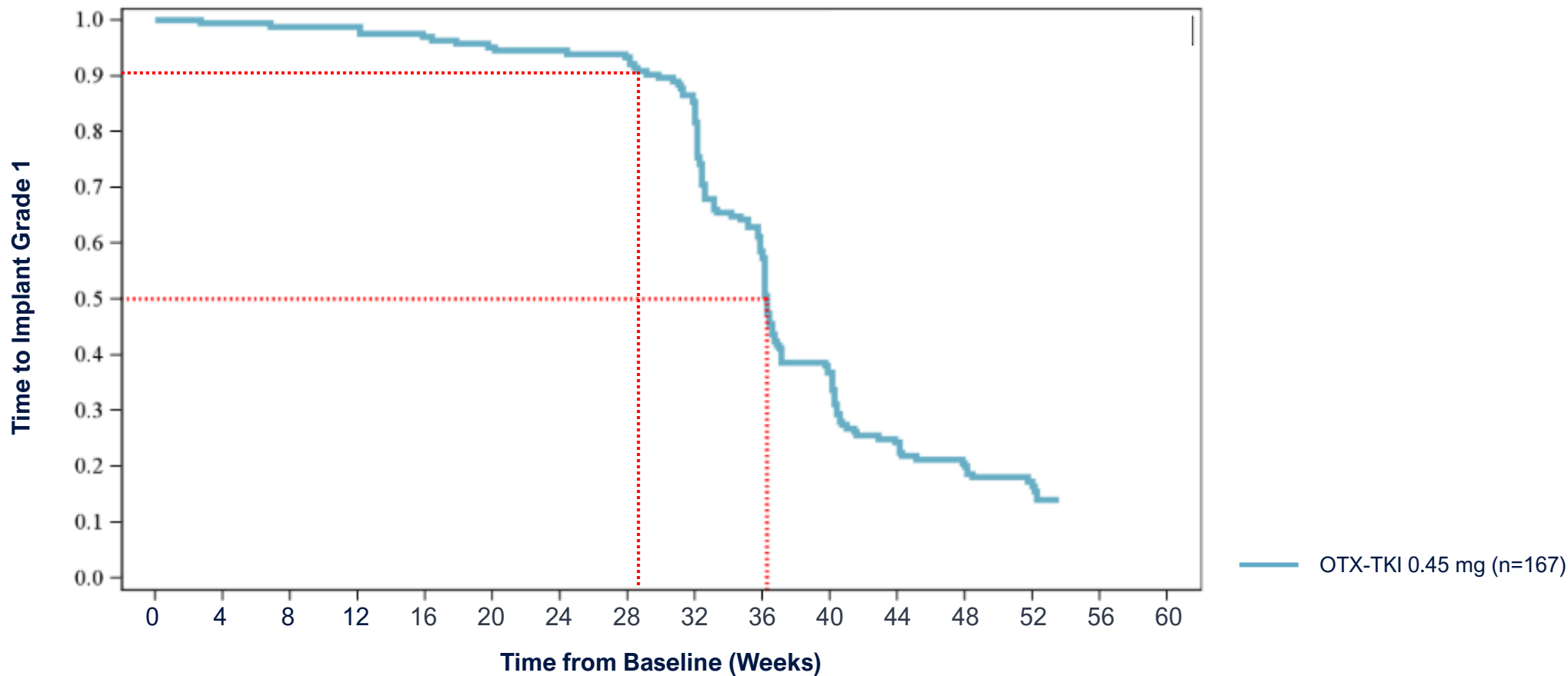
*Maintenance of vision defined as proportion of subjects who maintain visual acuity, a loss of <15 ETDRS letters of BCVA from baseline. Predefined statistical rules were applied to adjust for treatment discontinuation or deviation as per the pre-specified statistical analysis plan. Full analysis set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

What is Driving this Sustained Durability?

*How May Early Fluid Control Inform Treatment
Decisions in Clinical Practice?*

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

Post Hoc Analysis: Time to Hydrogel Dissipation



**Axitinib release is sustained throughout the period of hydrogel persistence
Residual drug particles continue to provide therapeutic effects for several weeks**

Kaplan-Meier analysis of time from Day 1 administration to the first Grade 1 implant assessment. Implant status was evaluated at scheduled study visits. Grade 3 indicates that the hydrogel implant remained fully intact, with the drug contained within the implant; Grade 2 indicates that the hydrogel implant had partially dissipated; and Grade 1 indicates that the hydrogel had fully dissipated, with released drug particles visible outside the implant in a localized or dispersed pattern.
1. Data on File 033. Ocular Therapeutix.

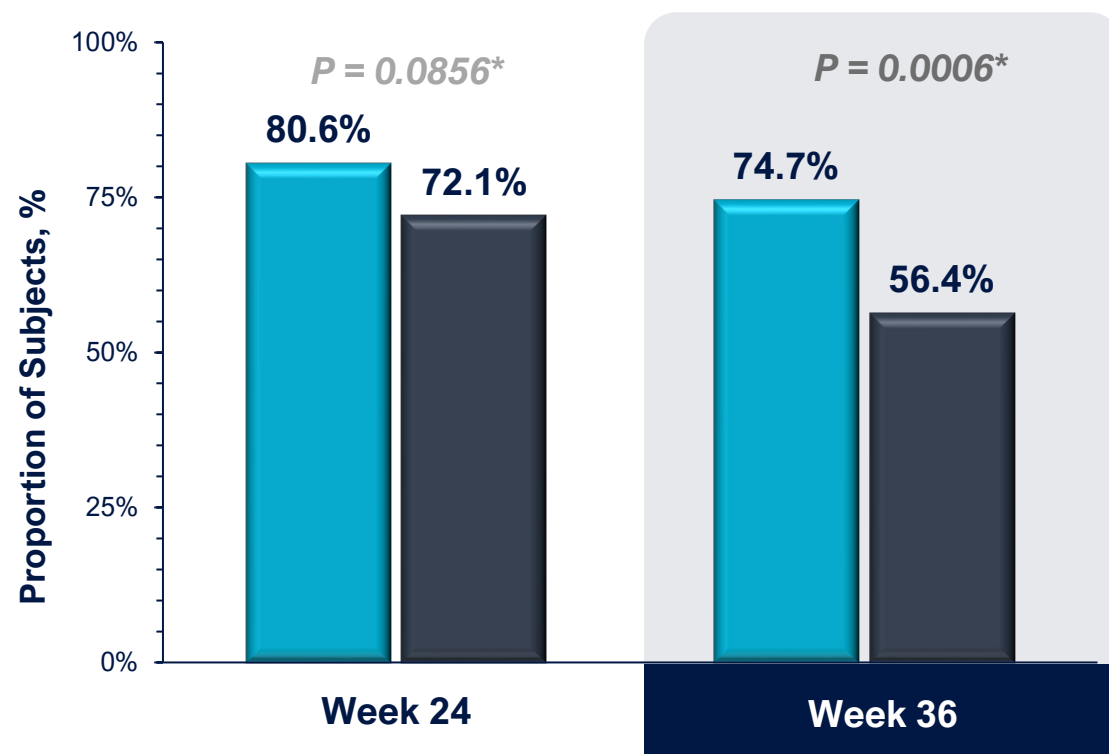
What is Driving this Sustained Durability?

***How May Early Fluid Control Inform Treatment
Decisions in Clinical Practice?***

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

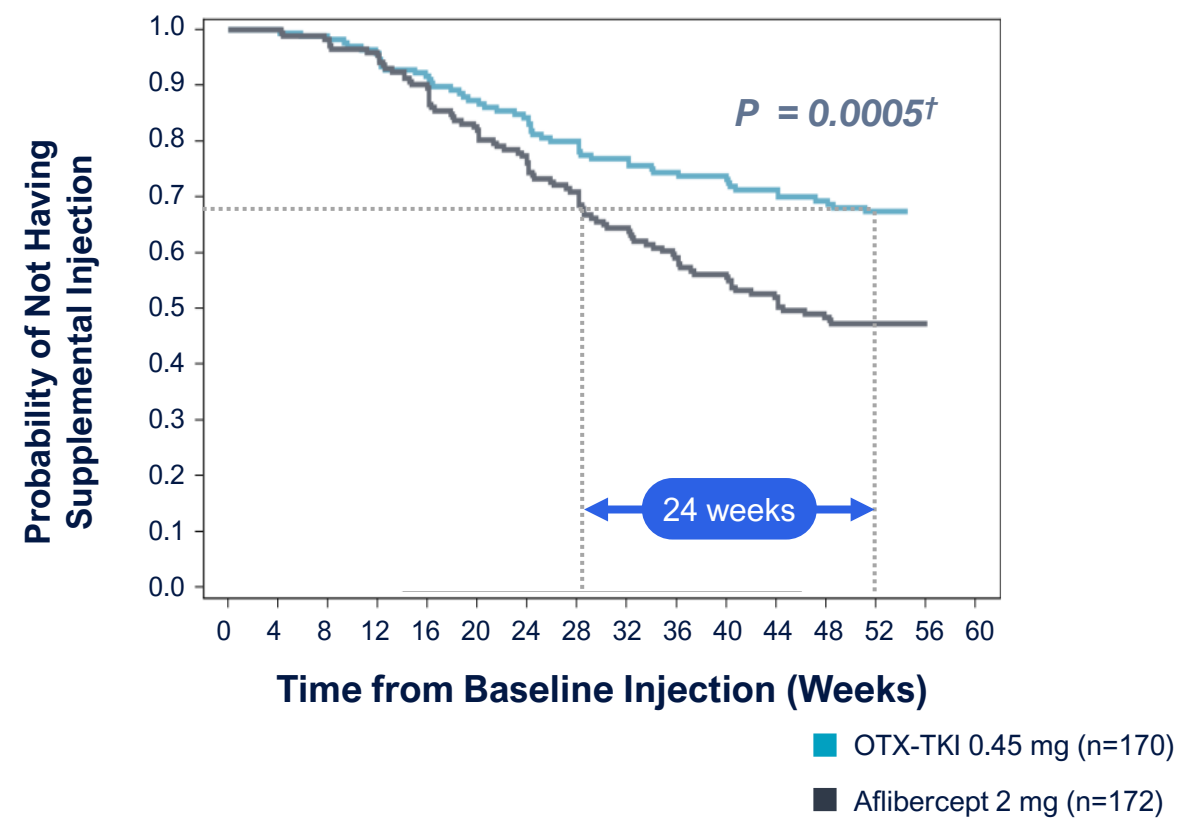
Proportion of Supplemental-free Subjects

Post Hoc Analysis



Time to First Supplemental Treatment

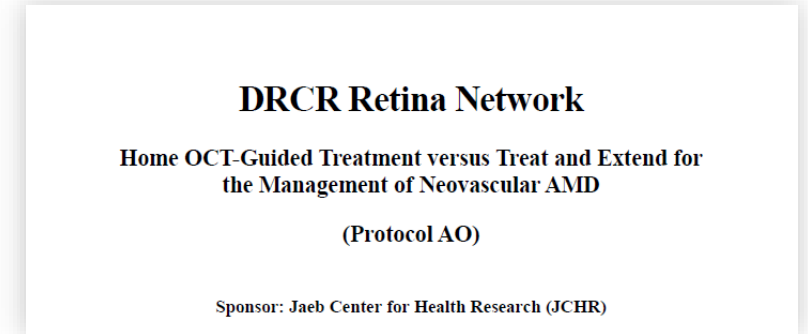
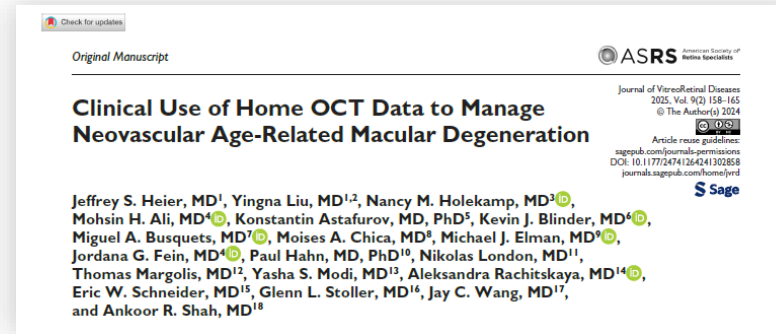
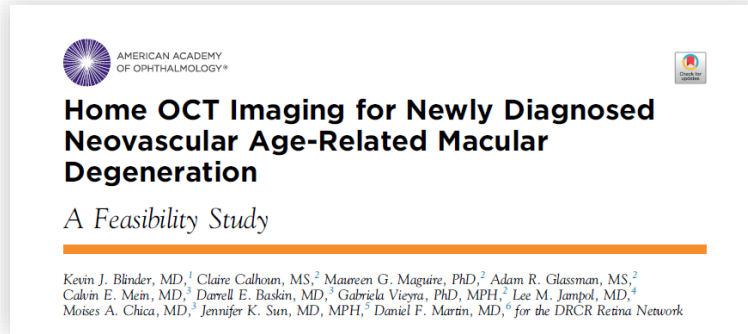
Secondary Endpoint



Predefined statistical rules were applied to adjust for treatment discontinuation or deviation as per the pre-specified statistical analysis plan. Full analysis set. Supplemental-free subjects include those who did not require rescue injections as specified by the protocol. At Week 52, the proportion of supplemental-free subjects was 68.8% in the OTX-TKI arm and 47.7% in the aflibercept 2mg arm

*Descriptive p-values; † Nominal P value; Suppl, supplemental

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



Defines Quantitative Dryness

≤10 nL of total retinal fluid was used as the definition of a dry retina¹

Clinically Relevant

10 nL was the median total retinal fluid notification threshold selected by 15 retina specialists²

Implemented Prospectively

DRCR Protocol AO uses 10 nL as the total retinal fluid threshold that triggers an office visit³

Quantitative dryness (qDry) defined as total IRF + SRF ≤10 nL

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

Most Patients in SOL-1 Demonstrated Retinal Fluid Control with AI-based Retinal Fluid Analysis

Post Hoc Analysis: Patients with *q*Dry Retina at Week 8

Change in Fluid Volume from Baseline at Week 8	OTX-TKI 0.45 mg N = 170	Aflibercept 2 mg N = 172
≤10 nL increase (<i>q</i> Dry Retina)	120 (70.6%)	129 (75.0%)
>10 nL increase	44 (25.9%)	36 (20.9%)
Missing data	6 (3.5%)	7 (4.1%)

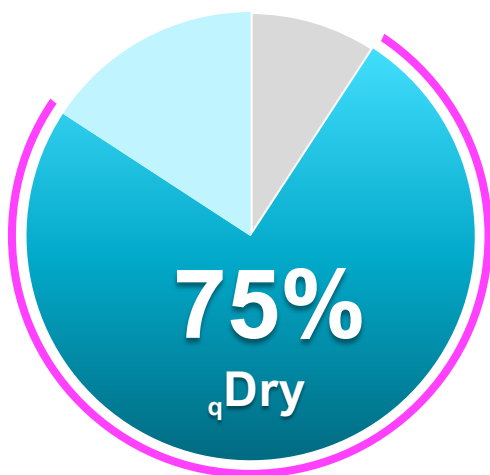
Using Real-world AI-based Retreatment Criteria, 2/3 of OTX-TKI Patients Would Achieve 9-month dosing

SOL-1

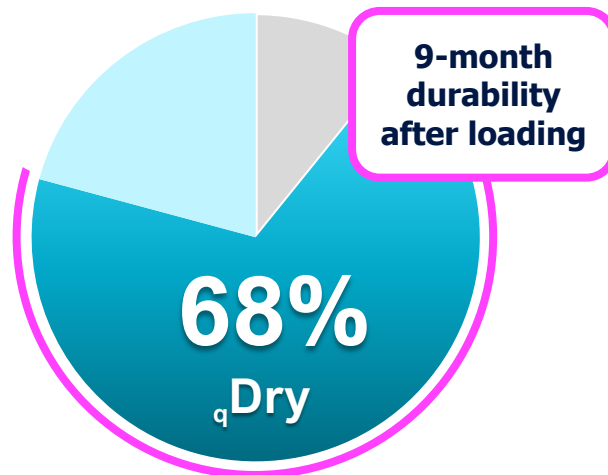
Post Hoc Analysis: Patients with _qDry Retina at Week 8

OTX-TKI 0.45 mg

Week 24



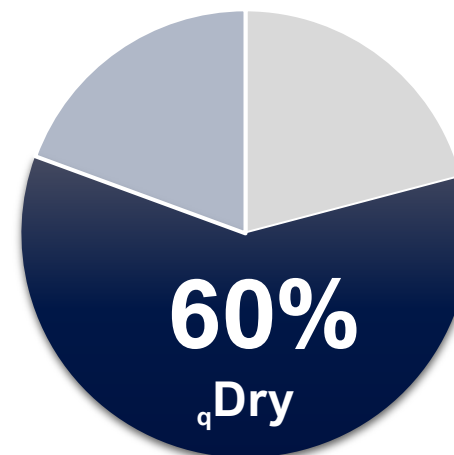
Week 36



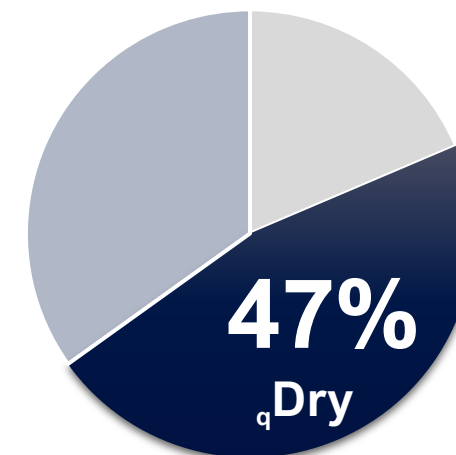
● ≤10nL increase ● >10nL increase ● Missing Data

Aflibercept 2mg

Week 24



Week 36

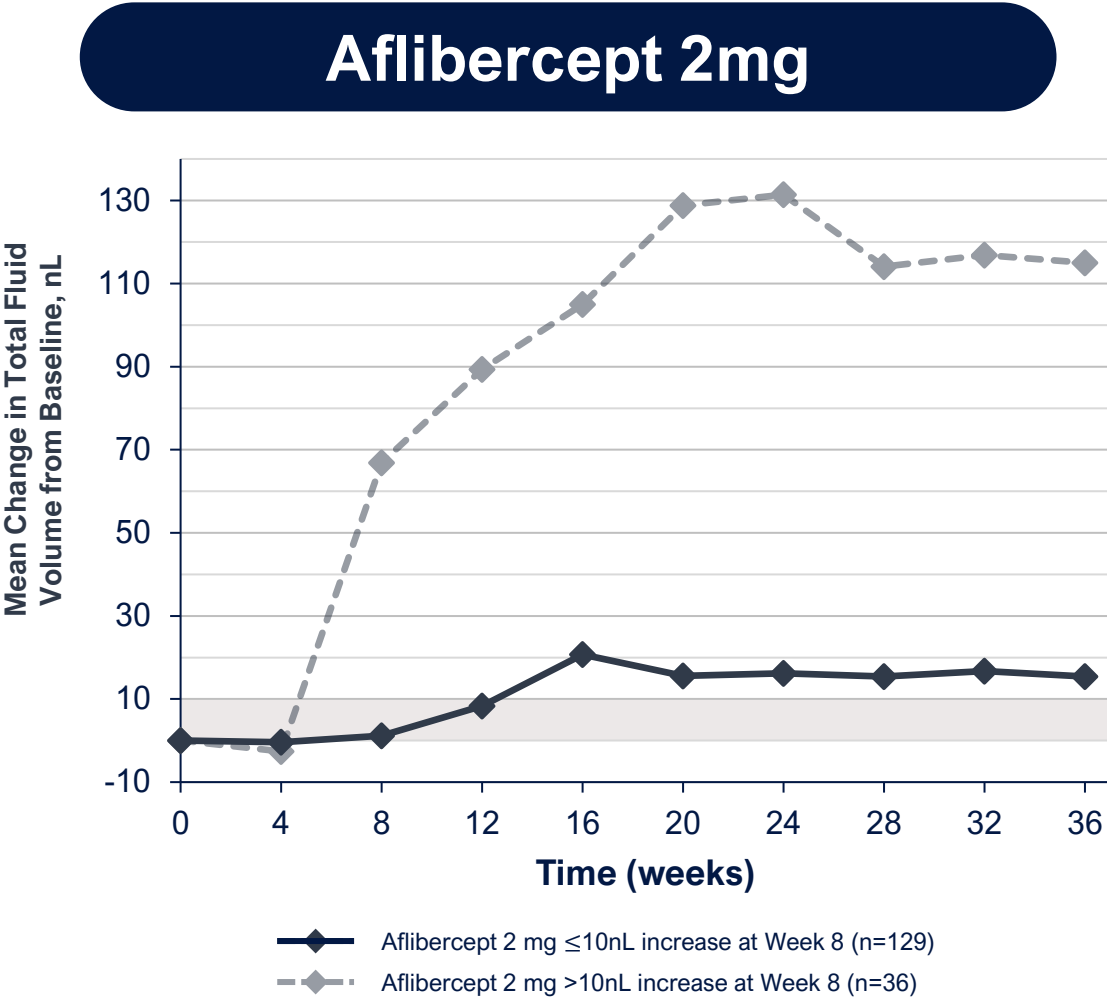
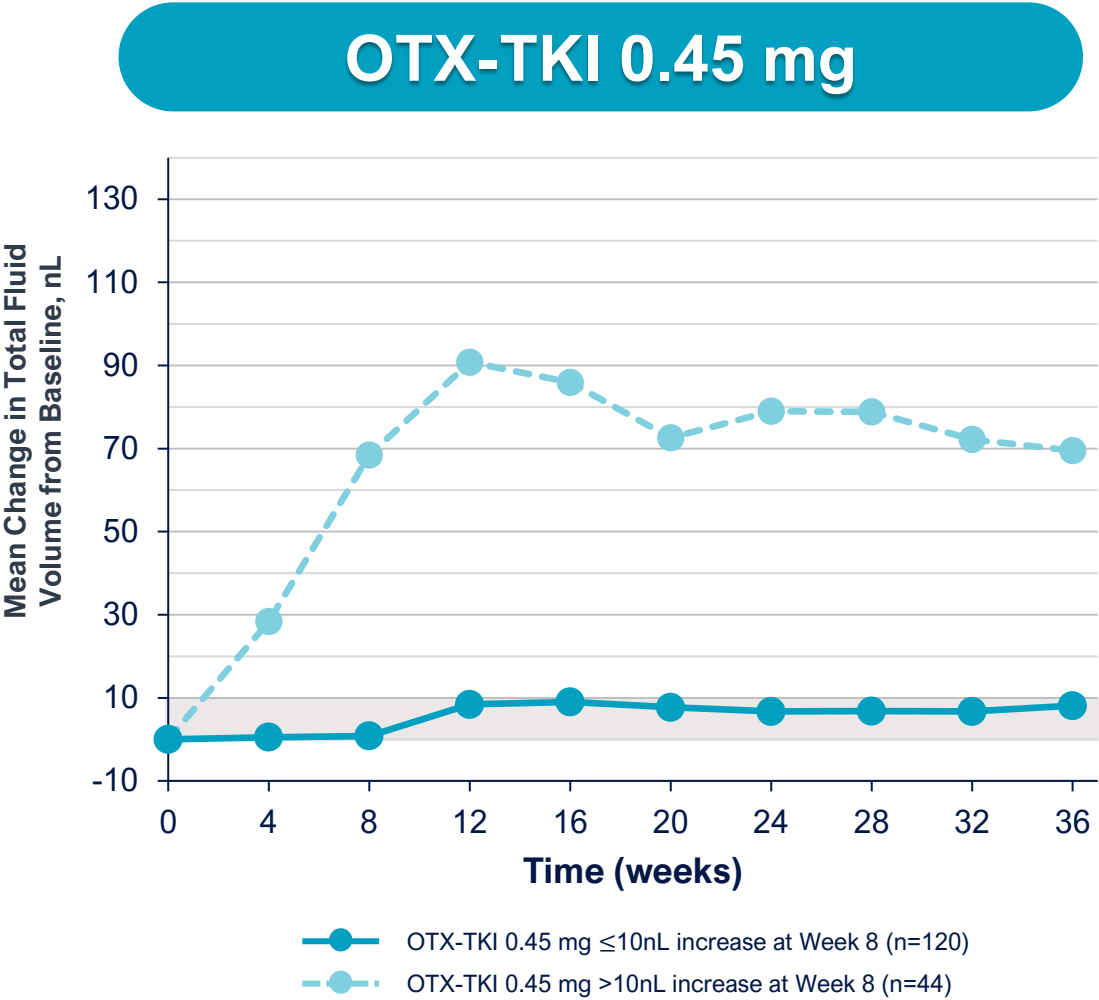


● ≤10nL increase ● >10nL increase ● Missing Data

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



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

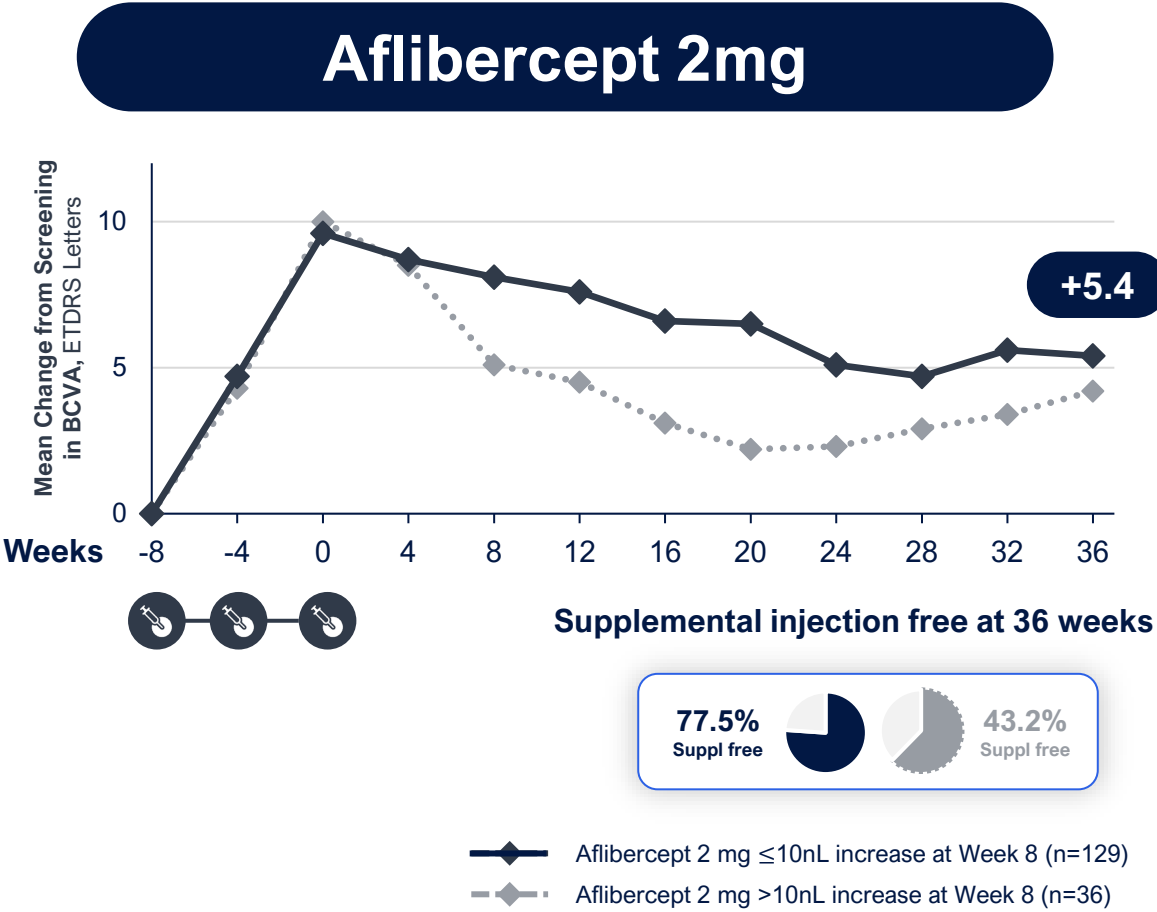
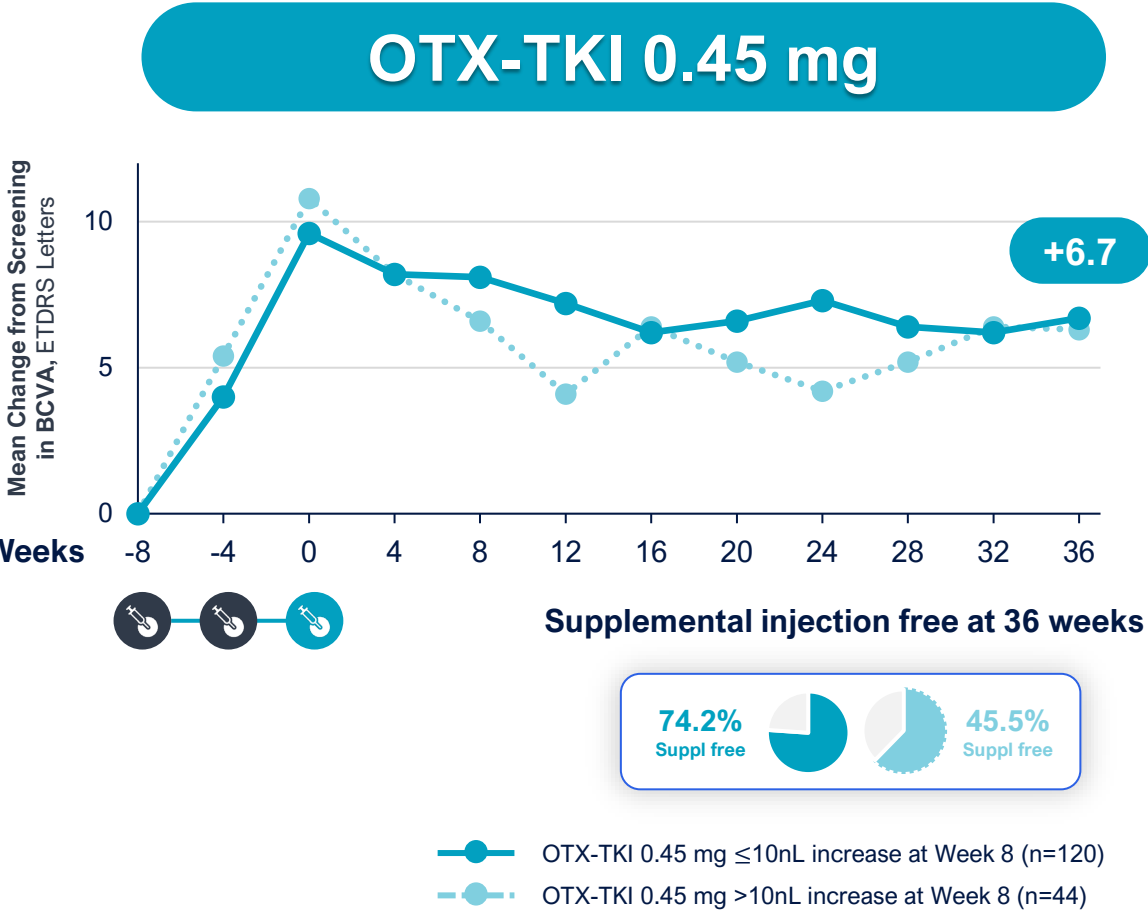


Quantitative dryness (qDry) defined as total intraretinal fluid and subretinal fluid volume ≤10 nL on AI (artificial intelligence)-based OCT evaluation with manual grader correction of retinal fluid performed at Boston Image Reading Center (BIRC). Analyses were based on observed cases; data were missing for 6 participants in the OTX-TKI arm and 7 in the aflibercept arm at Week 8. For participants who received rescue treatment on or before Week 52, fluid-volume measurements obtained after the first rescue injection were treated as missing.

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

SOL-1

Post Hoc Analysis: Mean BCVA Change by qDry Status at Week 8



Quantitative dryness (qDry) defined as total intraretinal fluid and subretinal fluid volume ≤ 10 nL on AI (artificial intelligence)-based OCT evaluation with manual grader correction of retinal fluid performed at Boston Image Reading Center (BIRC). Analyses were based on observed cases; data were missing for 6 participants in the OTX-TKI arm and 7 in the aflibercept arm at Week 8. For participants who received supplemental treatment on or before Week 52, fluid-volume measurements obtained after the first supplemental injection were treated as missing. Supplement-free subjects include those who did not require rescue injections as specified by the protocol. BCVA, best corrected visual acuity; ETDRS, early treatment diabetic retinopathy study;

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OTX-TKI was Generally Well Tolerated

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

Vitreous Floaters

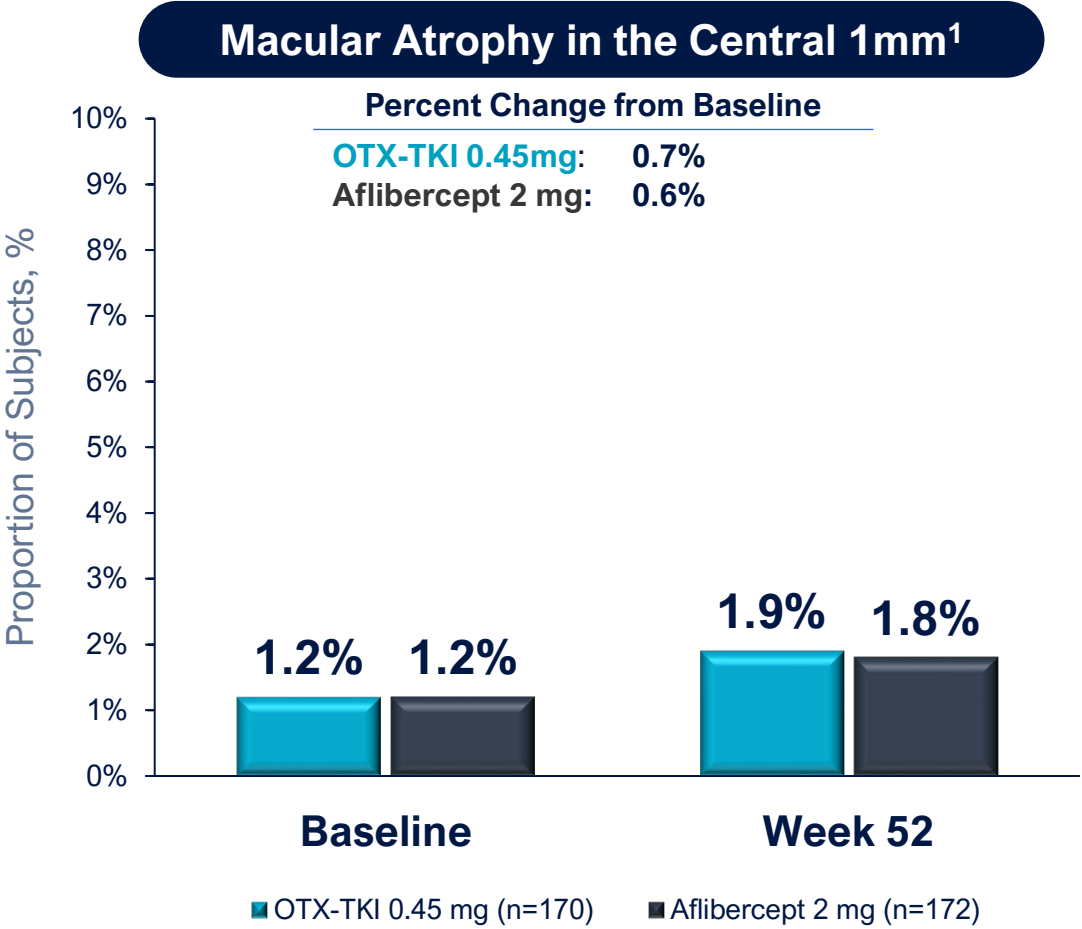
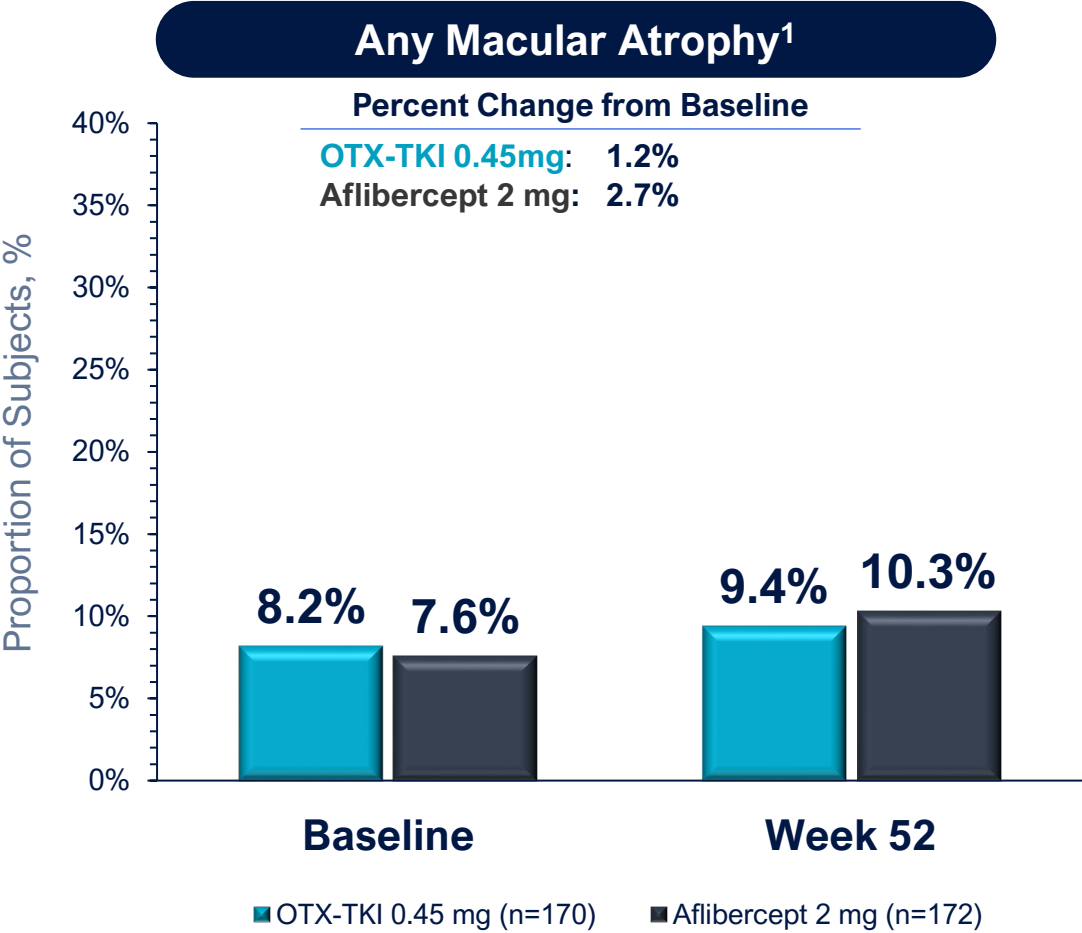
- All cases were mild to moderate in severity
- No evidence of associated IOI
- Onset coincides with drug elution stage of OTX-TKI hydrogel bioresorption process
- For all subjects with vitreous floaters AE reported, drug particles are no longer visible

Intraocular Inflammation

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

Incidence of Macular Atrophy in SOL-1

Safety Analysis



¹cRORA measured by the reading center
cRORA, complete retinal pigment epithelium and outer retinal atrophy

Key Takeaways

SOL-1 **met its primary endpoint**, demonstrating superiority vs. aflibercept 2 mg in maintenance of visual acuity at Week 36

OTX-TKI hydrogel remained visible in **>90% of patients at Month 6** and ~50% at Month 9

~70% of OTX-TKI treated subjects quantitatively dry at Week 8 continued to be **quantitatively dry through Week 36**

OTX-TKI was **generally well-tolerated** through Week 52; long-term follow-up continues through end of Year 2

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