Ocular Therapeutix: Redefining the Retina Experience

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Chief Scientific Officer

OCULAR THERAPEUTIX

Retina experience redefined

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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 investigational product candidate AXPAXLI (also known as OTX-TKI), including the Company's intention to submit a new drug application for AXPAXLI for the treatment of wet AMD based on Week 52 efficacy and safety data from the Company's SOL-1 Phase 3 clinical trial, Week 52 data from an interim safety analysis to be conducted in the Company's SOL-R clinical trial, and confirmatory evidence; statements regarding the timing, design, enrollment, randomization, conduct and retention of subjects in the Company's ongoing and planned clinical trials for AXPAXLI; statements regarding the likelihood of success of the Company's SOL-R trial; statements regarding the Company's hypotheses regarding design factors relevant to the success of clinical trials; statements regarding the potential utility or adoption, if approved, of any of the Company's product candidates, including AXPAXLI; and other statements containing the words "anticipate", "believe", "estimate", "expect", "intend", "designed", "goal", "may", "might", "plan", "position", "predict", "project", "target", "potential", "will", "would", "could", "should", "continue", and similar expressions, all of which constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors. Such forward-looking statements involve substantial risks and uncertainties that could cause the Company's development programs, future results, performance, or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, uncertainties regarding the initiation, design, timing, conduct and outcomes of the Company's ongoing clinical trials, including the Company's SOL-1 trial, SOL-R trial, HELIOS-3 trial, and SOL-X trial; uncertainty as to whether the data from earlier clinical trials will be predictive of the data of later clinical trials, particularly later clinical trials that have a different design or utilize a different formulation than the earlier trials, whether preliminary or interim data from a clinical trial or post-hoc analyses of clinical data will be predictive of final data from such trial, or whether data from a clinical trial assessing a product candidate for one indication or patient population will be predictive of results in other indications or patient populations; availability of data from clinical trials and expectations for regulatory submissions and approvals; the Company's scientific approach and general development progress; and other factors discussed in the "Risk Factors" section contained in the Company's quarterly and annual reports on file with the Securities and Exchange Commission. In addition, the forward-looking statements included in this presentation release represent the Company's views as of the date of this presentation. The Company anticipates that subsequent events and developments may cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so, whether as a result of new information, future events or otherwise, except as required by law. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this presentation.

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This presentation discusses investigational product candidates in development, including OTX-TKI. Their efficacy and safety profiles have not been established, and they have not been approved for marketing by the FDA or any other regulatory agency.

OTX-TKI

A Distinct TKI Program



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Evaluating Retinal TKIs From OCUL Perspective

Core TKI Considerations

Axitinib is the most potent TKI for VEGFRs in Wet AMD Development[2,7,8]

Axitinib is 100x more potent than Vorolanib for VEGFR-2

Hydrogel Technology Developed to Optimize Sustained Release PK

TKI Receptor Inhibition at Physiologic Testing Conditions *In Vitro**

Kinase[1,2]	Axitinib	Vorolanib[3-5]	Sunitinib
VEGF RECEPTORS			
VEGFR-1	99%	39%	83%
VEGFR-2	97%	28%	71%
VEGFR-3	95%	59%	72%
OTHER RECEPTORS			
PDGFR-α	79%	42%	70%
PDGFR-β	88%	41%	87%
FGFR-1	76%	0%	45%
FGFR-2	76%	16%	54%
FGFR-3	67%	15%	63%
JAK-1	18%	13%	52%

Inhibition Key: <50% 50-70% 70-85% 85-100%

Physiologic test conditions include 1mM ATP. Axitinib intraocular concentrations = 1.03 to 1.13 µM; Vorolanib intraocular concentrations = 0.23 to 0.95 µM[3,4,6]

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*Kinome Tree inhibition analysis conducted in collaboration with AssayQuant. PhosphoSens® assay (AssayQuant®) conducted at 1mM ATP and 1µM drug concentrations.

1. Data on file, Ocular Therapeutix. 2. Patel C, et al. Target and Selectivity Profiling of Axitinib in Cell-Based and Biochemical Assays. Presented at the Association for Research in Vision and Ophthalmology. May 8, 2025, Salt Lake City, UT. 3. Singh RP, et al. A 12-Month, Ocular Pharmacokinetic Study of EYP-1901, a Sustained-release, Intravitreal Formulation of the Tyrosine Kinase Inhibitor Vorolanib. Presented at the American Society of Retina Specialists Annual Meeting; July 28–August 1, 2023; Seattle, WA; 4. Kupperman BD, et al. Poster B0301. Presented at ARVO 2024 Annual Meeting, May 5–9, 2024; Seattle, WA; 5. Xiu X, et al. *Organic Process Research & Development*. 2024;28(2):492-499; 6. Saim, S., Howard-Sparks, M., Paggiarino, D., Karzoun, B. and Chen, J., Eyepoint Pharmaceuticals Inc, 2026. Bioerodible ocular drug delivery insert and therapeutic method. U.S. Patent 12,551,368. 7. Blizzard, C et al. Pharmacodynamic efficacy of optimized intravitreal axitinib implant (OTX-TKI) in a VEGF challenge rabbit model. Presented at the Association in Vision and Ophthalmology. May 9, 2024. Seattle, WA, US. 8. Reaction Biology, Germany; Cellular Phosphorylation Assay Service. (https://www.reactionbiology.com) CHO Cellular assay data demonstrated no TIE2 inhibition within physiological drug solubility range at normal cellular ATP levels via the gold standard cell phosphorylation assay; Data on File 042. Ocular Therapeutix. 2026.

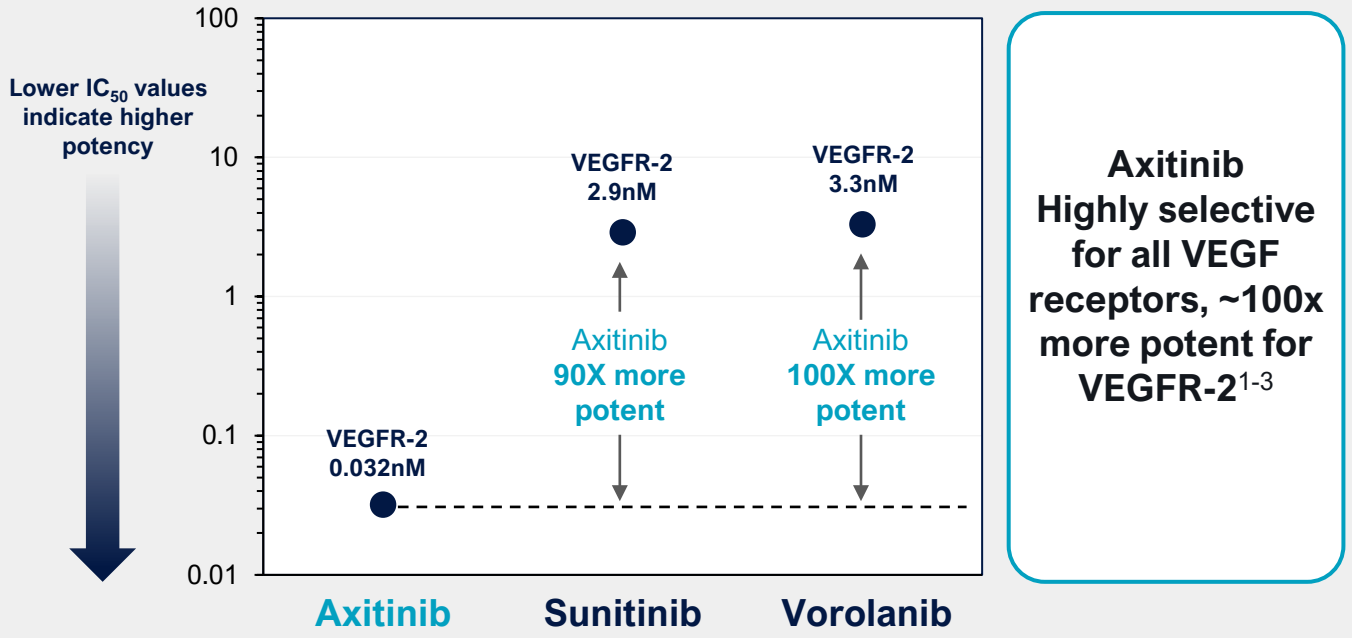
TKI, tyrosine kinase inhibitor; ATP, adenosine triphosphate; VEGFR, vascular endothelial growth factor receptor; PDGFR, platelet-derived growth factor receptor; FGFR, fibroblast growth factor receptor; JAK, janus kinase; AMD, age-related macular degeneration; PK, pharmacokinetics; OCUL, Ocular Therapeutix

Evaluating Retinal TKIs From OCUL Perspective

Core TKI Considerations

- Axitinib is the most potent TKI for VEGFRs in Wet AMD Development
- **Axitinib is 100x more potent than Vorolanib for VEGFR-2**[1-3]
- Hydrogel Technology Developed to Optimize Sustained Release PK

Retinal TKIs: IC_{50} for VEGFR-2 (nM)[1-3]



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

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VEGFR, vascular endothelial growth factor receptor; IC50, inhibitory concentration 50%; PK, pharmacokinetics; AMD, age-related macular degeneration; OCUL, Ocular Therapeutix

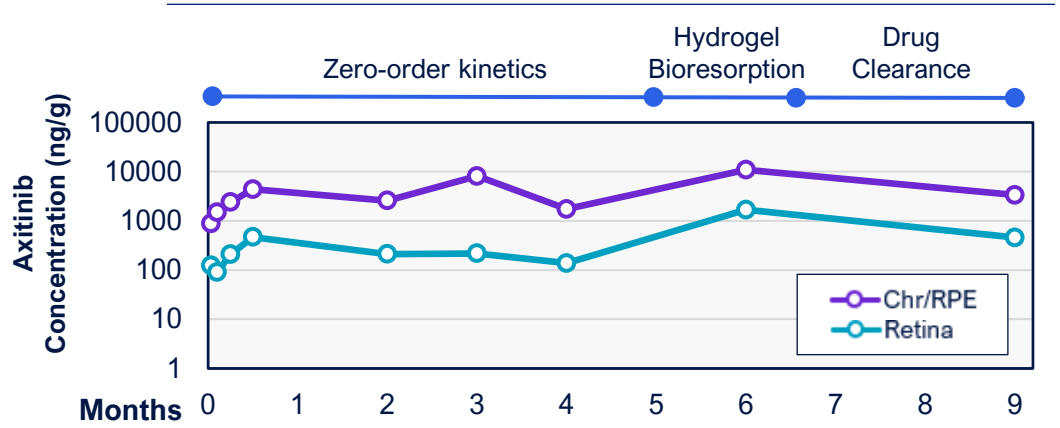
Evaluating Retinal TKIs From OCUL Perspective

Core TKI Considerations

- Axitinib is the most potent TKI for VEGFRs in Wet AMD Development
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- **Hydrogel Technology Developed to Optimize Sustained Release PK[1-3]**

Consistent Daily Release with OTX-TKI[1]

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



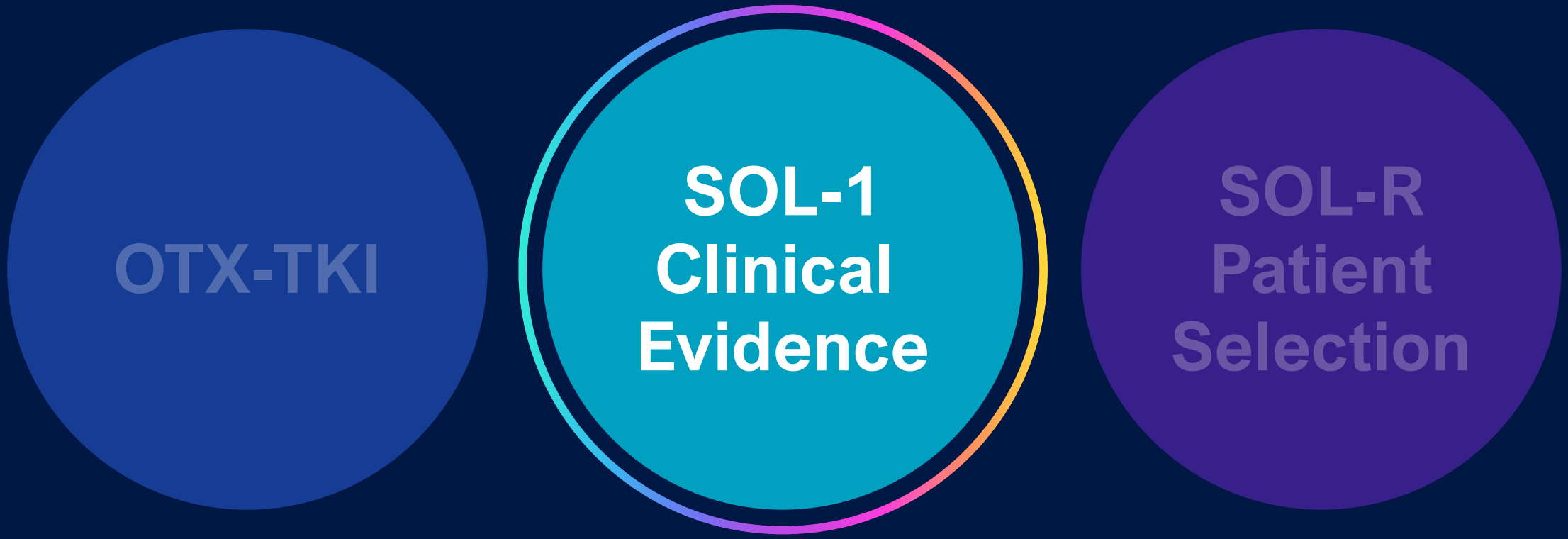
- Rapid, continuous and consistent axitinib delivery; targeted drug delivery to retina and choroid for 9-12 months

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1. Data on File 033. Ocular Therapeutix. 2. Blizzard CD, Driscoll A, El-Hayek R, et al. inventors; Ocular Therapeutix, Inc., assignee. Ocular implant containing a tyrosine kinase inhibitor. US patent 11,439,592 B2. September 13, 2022. 3. Blizzard, C et al. Pharmacodynamic efficacy of optimized intravitreal axitinib implant (OTX-TKI) in a VEGF challenge rabbit model. Presented at the Association in Vision and Ophthalmology. May 9, 2024. Seattle, WA,
Chr, choroid; RPE, retinal pigment epithelium; NHP, non-human primate; PK, Pharmacokinetics; OCUL, Ocular Therapeutix

OTX-TKI

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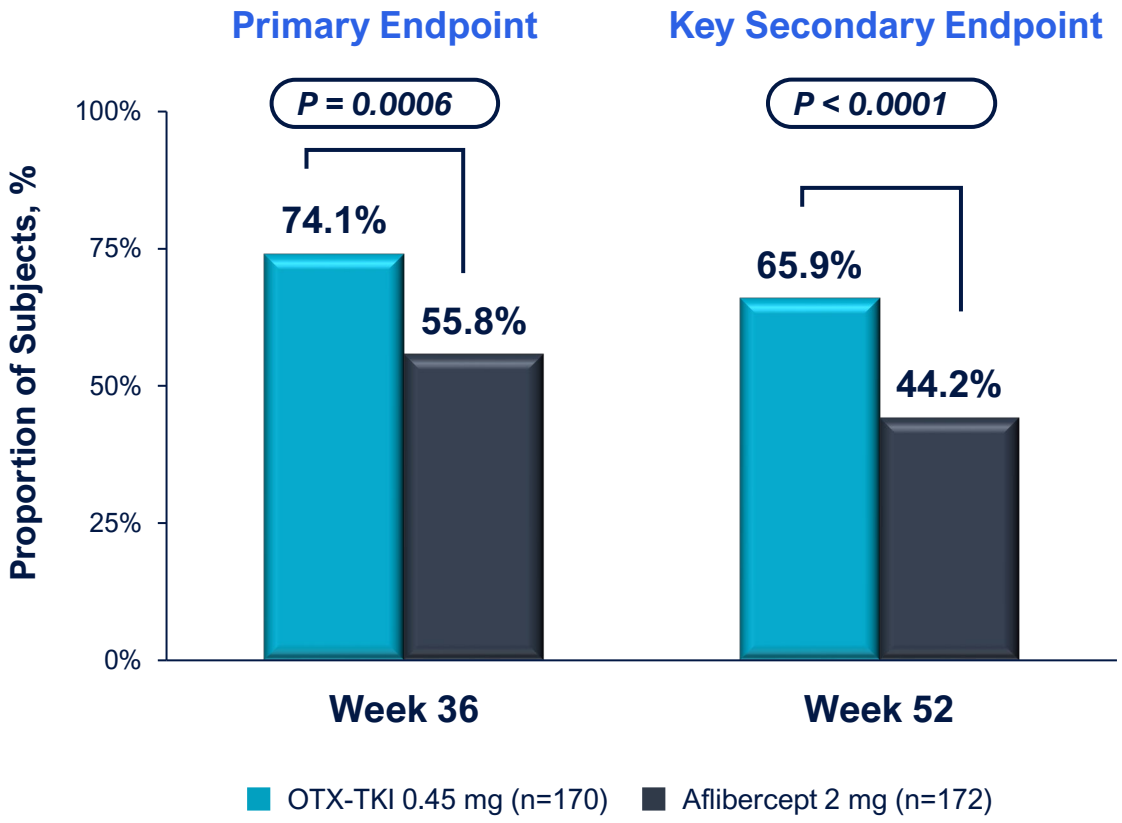
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SOL-1: First trial to demonstrate durability ≥ 9 months

SOL-1

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

Maintenance of Visual Acuity*



Ocular Adverse Events

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)

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

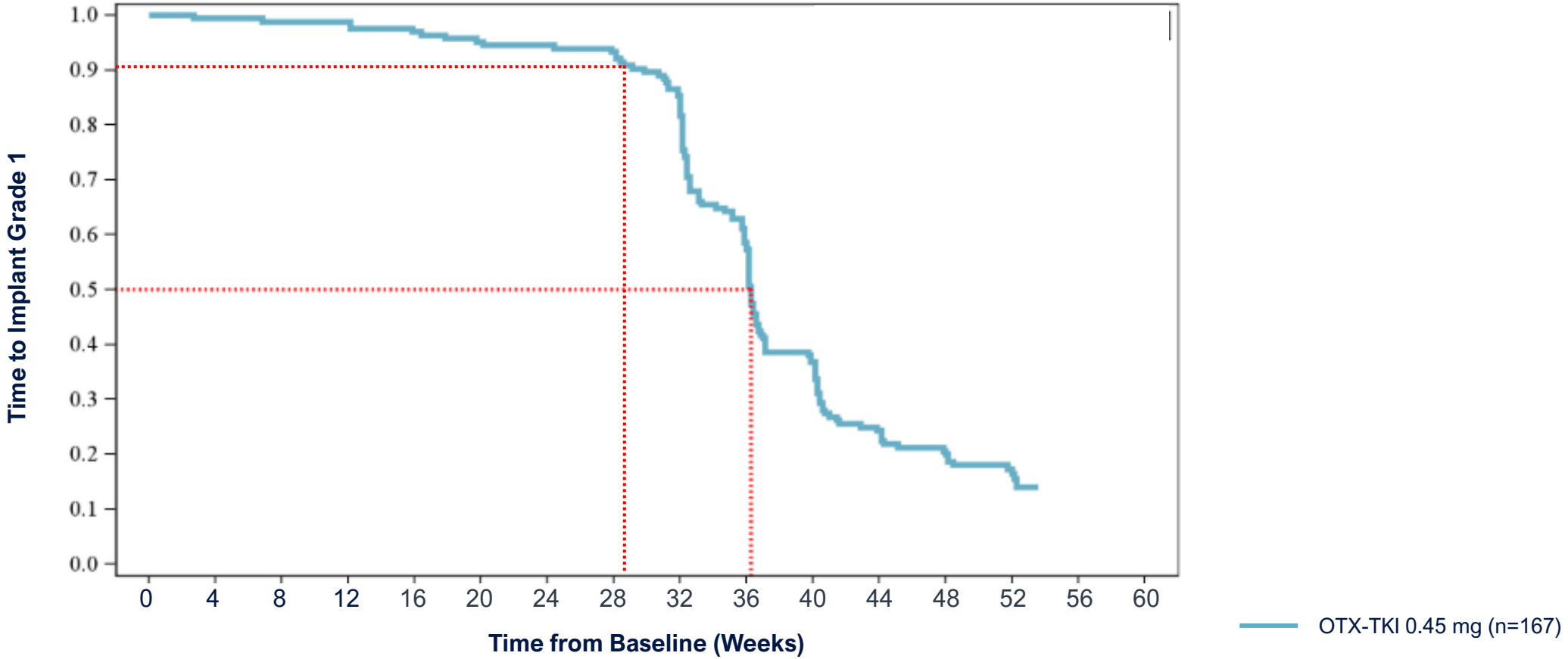
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*Maintenance of vision defined as proportion of subjects who maintain visual acuity, a loss of <15 ETDRS letters of BCVA from baseline
Predefined statistical rules were applied to adjust for treatment discontinuation or deviation as per the pre-specified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

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

SOL-1

Post Hoc Analysis: Time to Hydrogel Dissipation



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

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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.

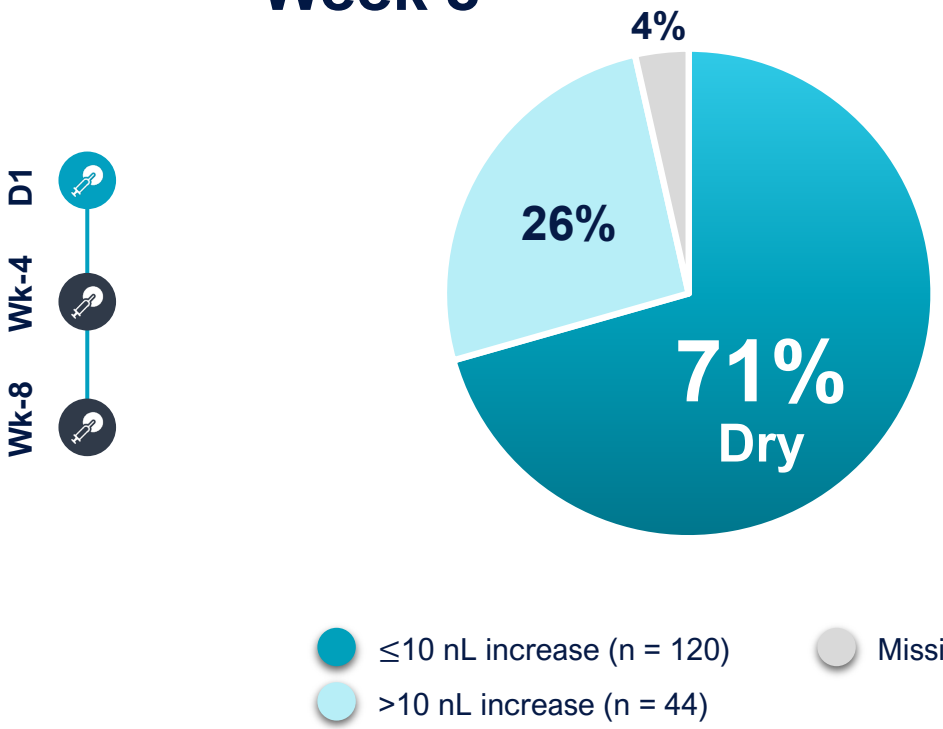
Most Patients in SOL-1 were Dry 8 weeks after Randomization with AI-based Retinal Fluid Analysis

Post Hoc Analysis: Quantitative Dry Retina Status at Week 8

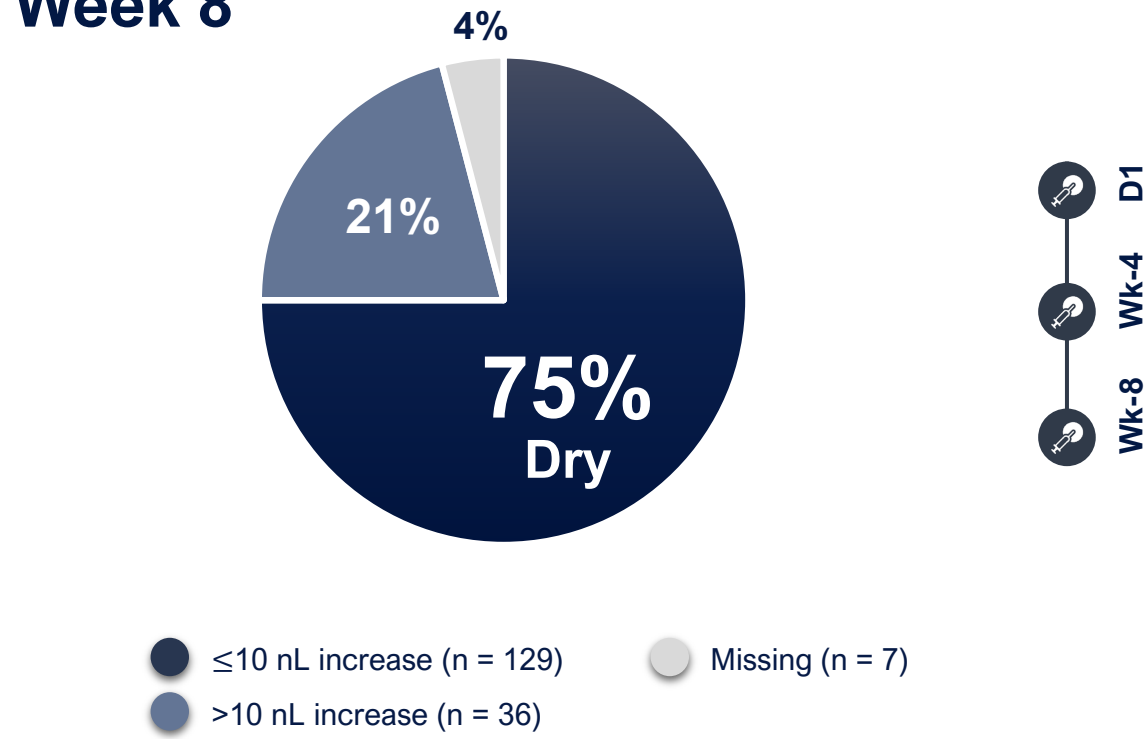
OTX-TKI 0.45 mg (N=170)

Aflibercept 2mg (N=172)

Week 8



Week 8



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

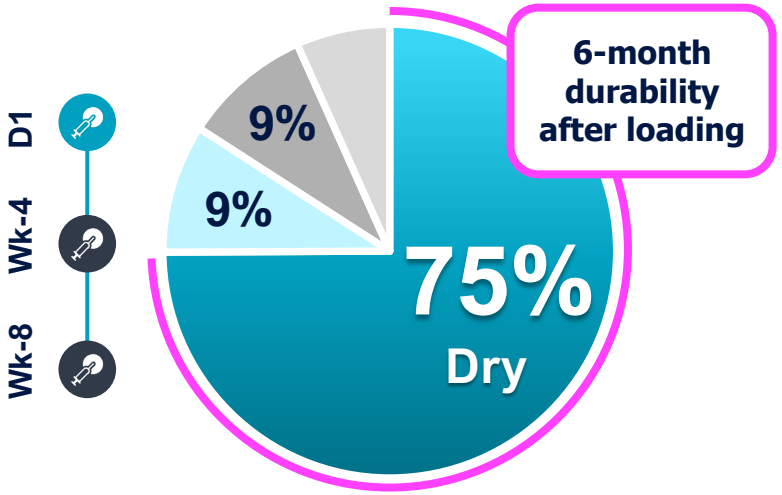
Using Real-World AI-based Retreatment Criteria, ~75% of OTX-TKI Patients Would Achieve 6-month Dosing*

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

SOL-1

OTX-TKI 0.45 mg (n=120)

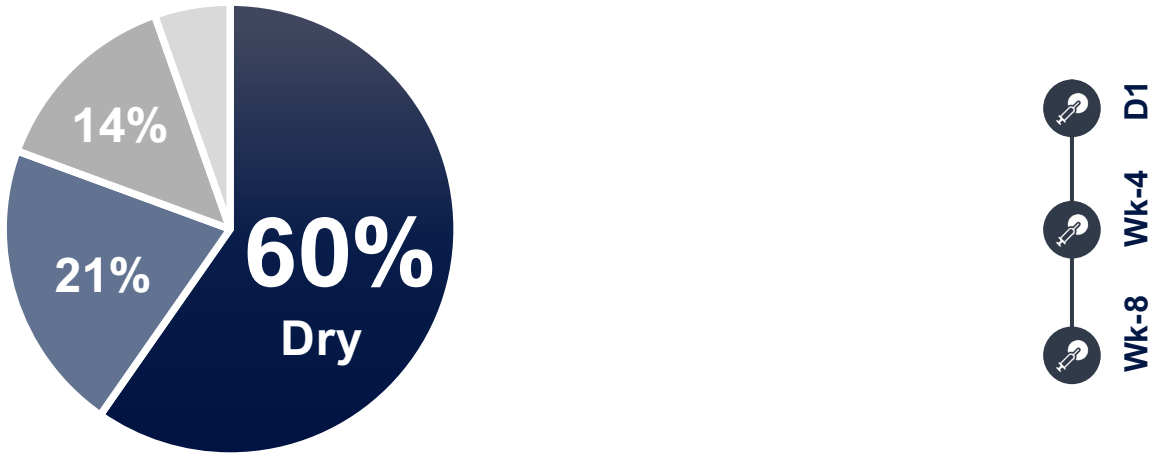
Week 24



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

Aflibercept 2mg (n=129)

Week 24



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

OCULAR THERAPEUTIX Retina experience redefined

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

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

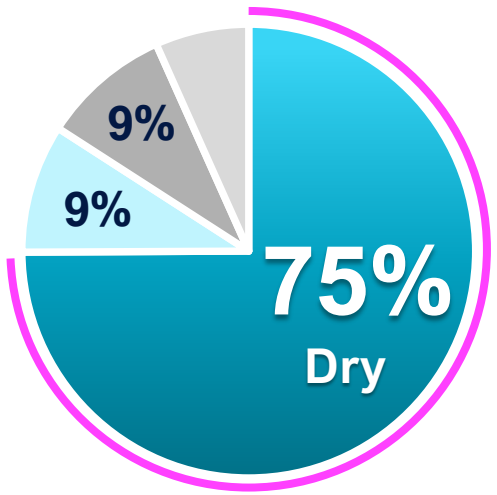
Post Hoc Analysis: Subgroup of patients with Quantitative Dry Retina at Week 8

SOL-1

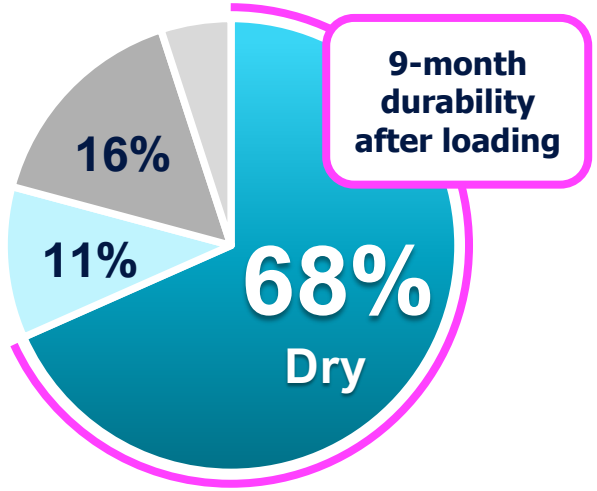
OTX-TKI 0.45 mg (n=120)

Aflibercept 2mg (n=129)

Week 24



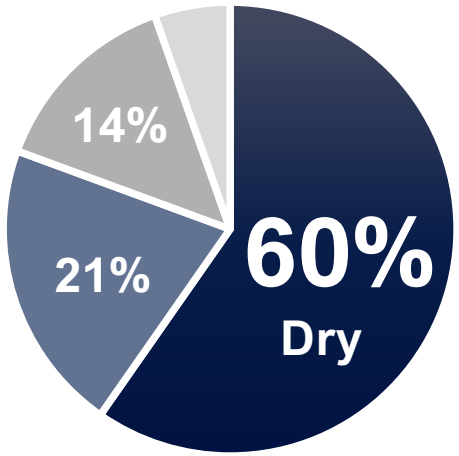
Week 36



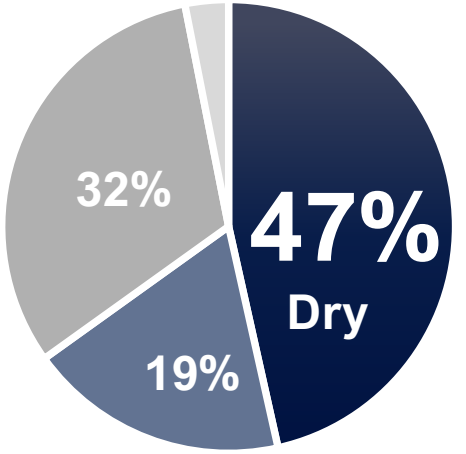
D1
Wk-4
Wk-8

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

Week 24



Week 36



D1
Wk-4
Wk-8

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

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Wk, week; D, day; nL, nanoliter; AI, artificial intelligence

OTX-TKI

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SOL-1 Clinical Evidence

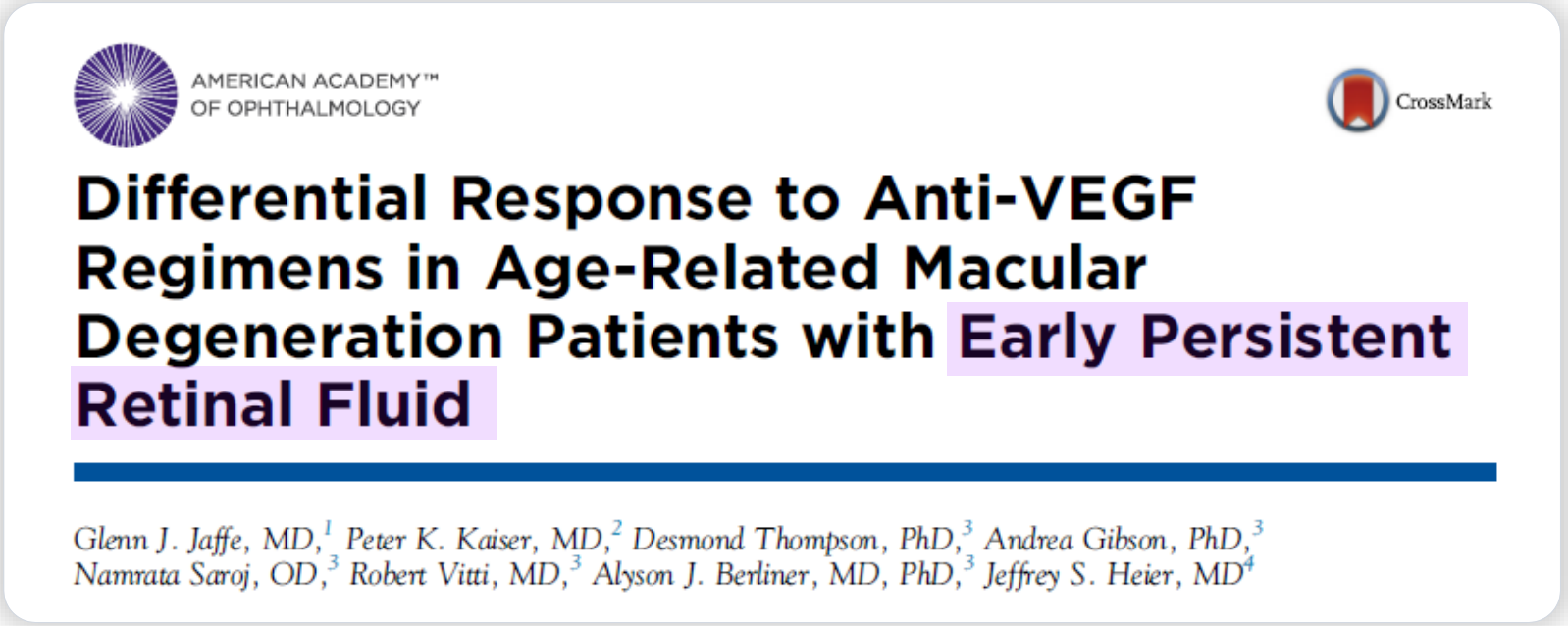
SOL-R Patient Selection

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Core Considerations in Wet AMD Patient Selection From OCUL Perspective

Wet AMD Patient Selection

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



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

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

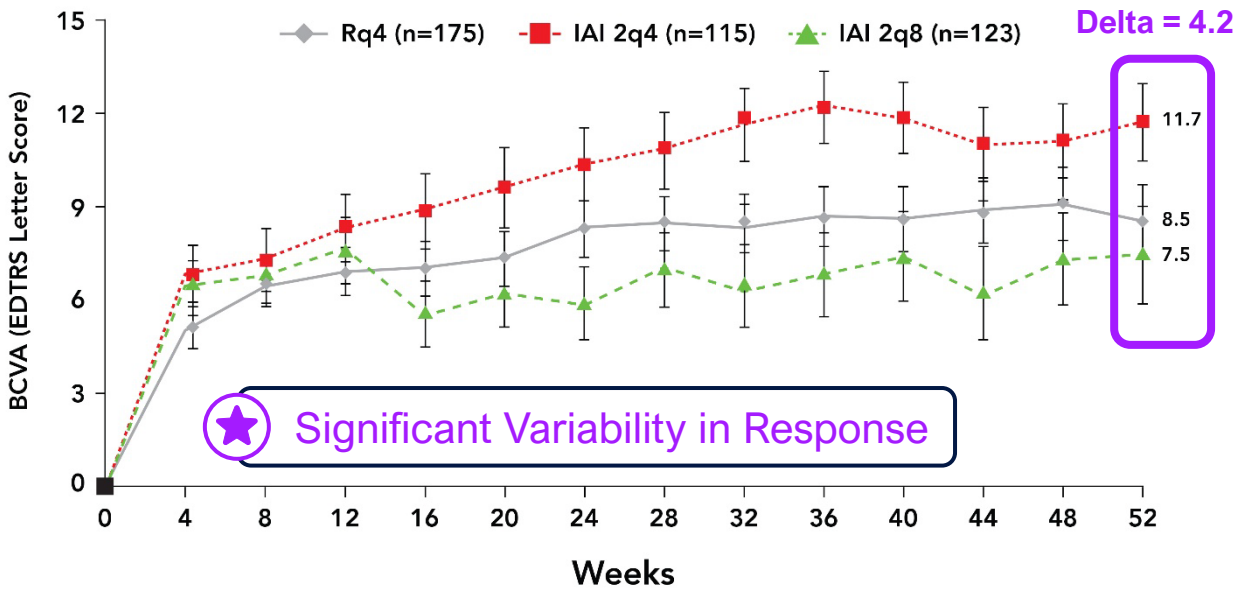
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1. Evans RN, et al. *JAMA Ophthalmol*. 2020;138(10):1043-1051; 2. Jaffe GJ, et al. *Ophthalmology*. 2016;123(9):1856-1864.
AMD, age-related macular degeneration; OCUL, Ocular Therapeutix

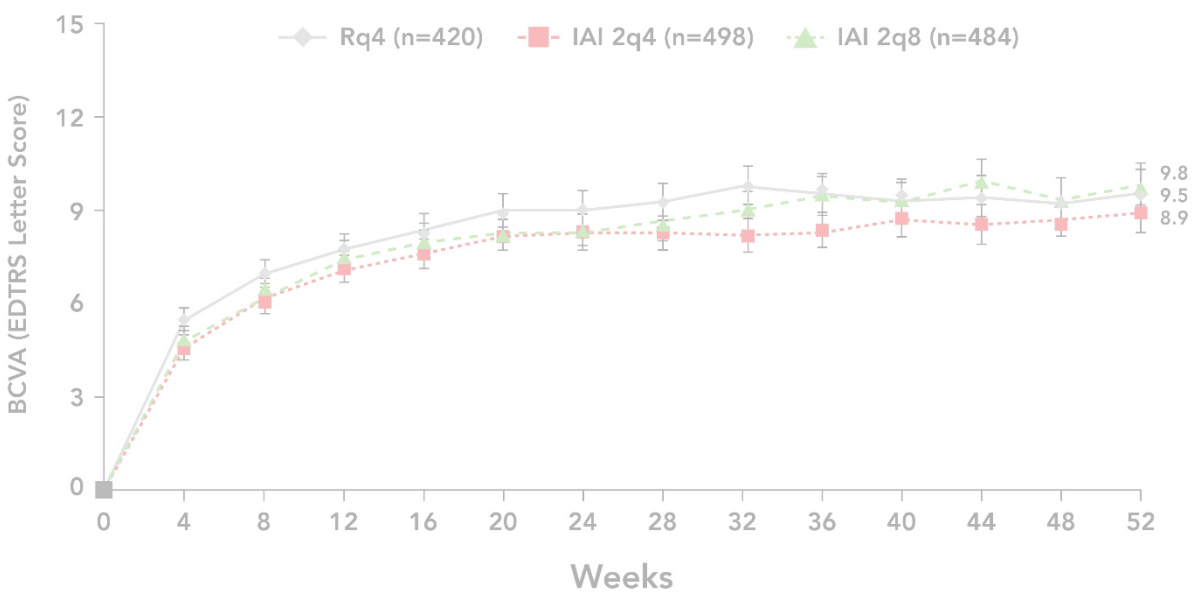
Patients with Early Persistent Fluid Can Disrupt Non-Inferiority Trials

Early persistent fluid patients are excluded from SOL-R

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



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



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

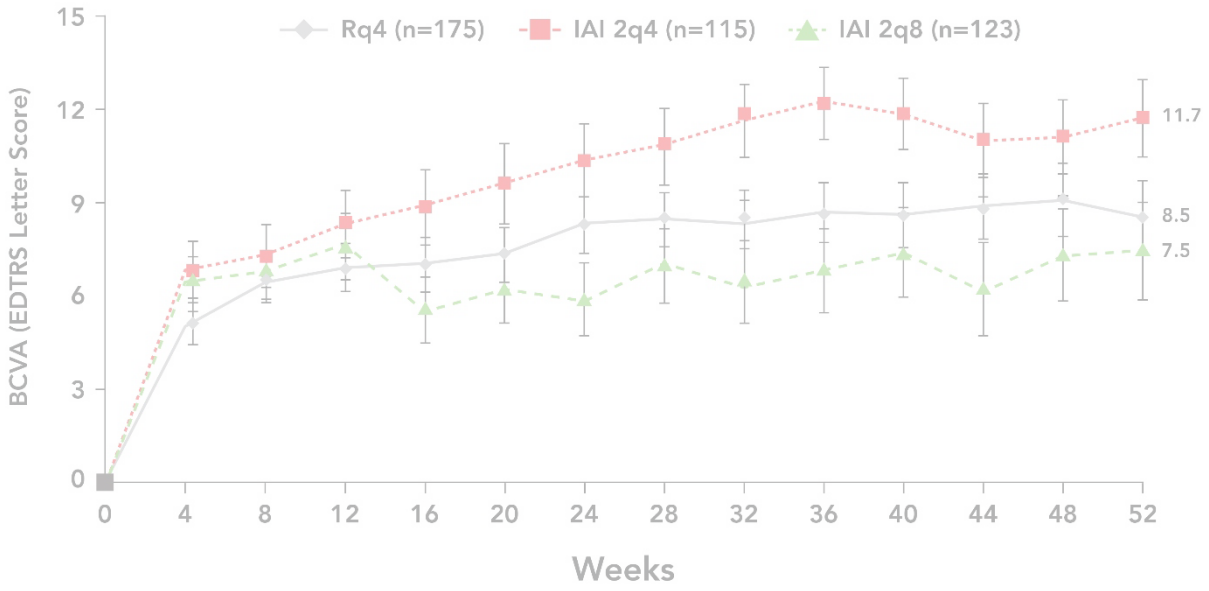
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Figures adapted from Jaffe et al.[1]
"Early Persistent Fluid" group captures patients that had retinal fluid as defined earlier on all initial 4 visits (baseline and weeks 4, 8, and 12). This period included all 3 visits during the initial loading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

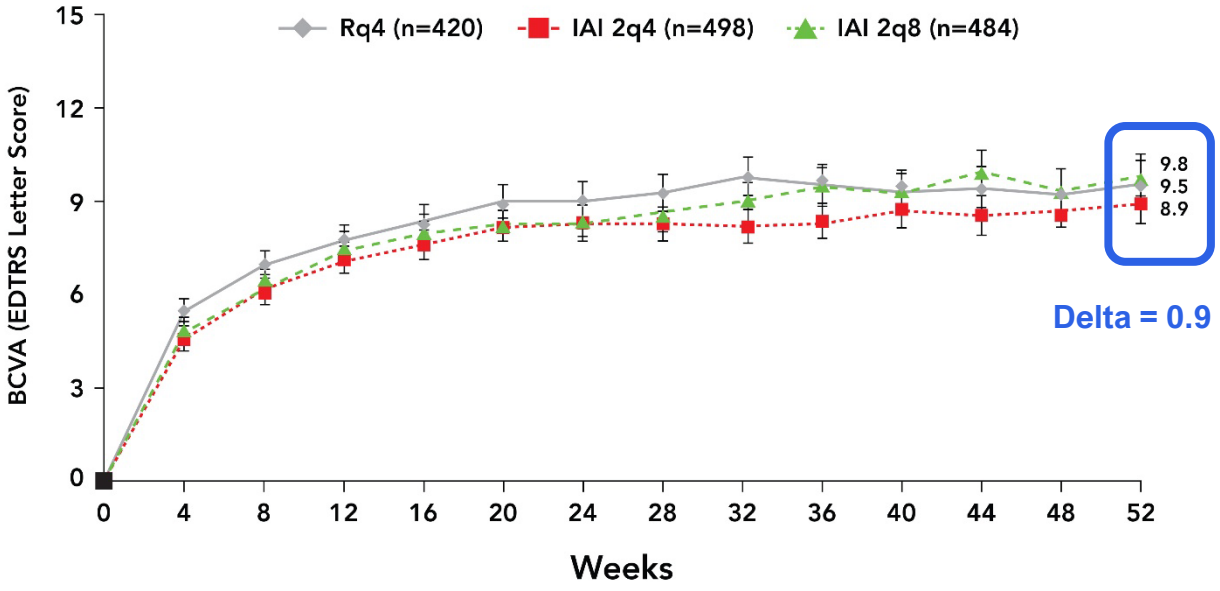
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✗ Vision in Patients *with* Early Persistent Fluid[1]



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



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

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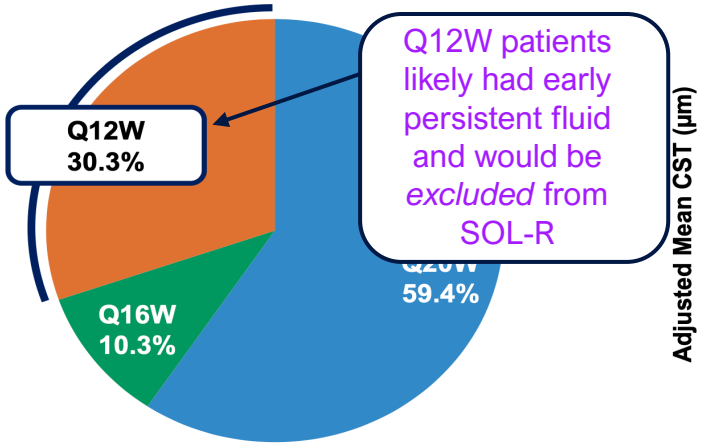
Figures adapted from Jaffe et al.[1]
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Lessons From KODIAK's DAZZLE Study: Rationale for SOL-R Patient Selection

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

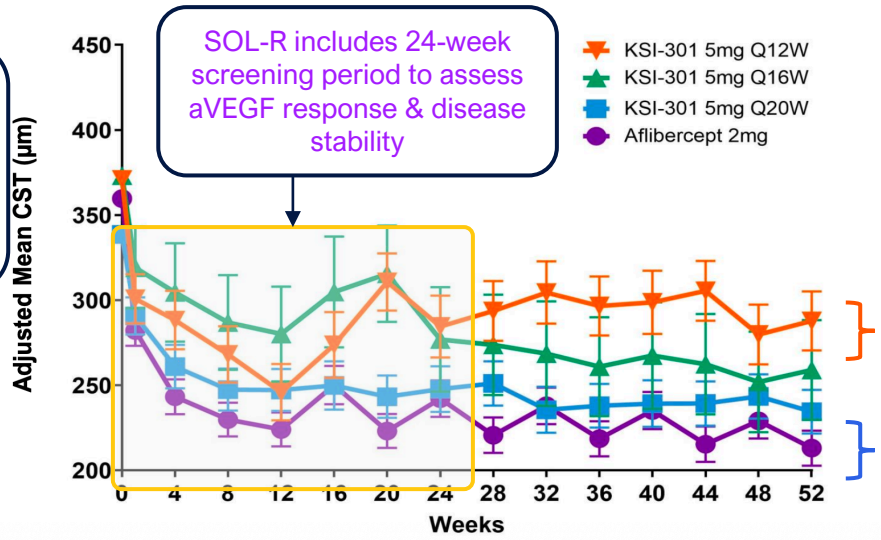
After the loading phase, the initial clinical effect deteriorated in the patients who met criteria for adjustment to the Q12W dosing interval, and subsequent Q12W dosing was insufficient

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



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

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



Unlikely SOL-R Patient

More likely SOL-R Patient

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

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

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

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

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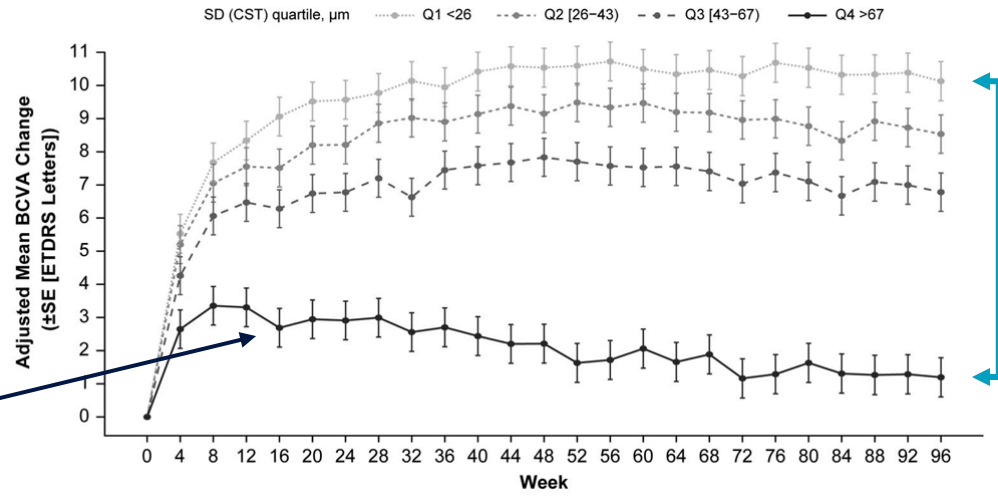
Greater Retinal Thickness Variability During Anti-VEGF Therapy is Associated with Suboptimal Anatomic and Visual Outcomes

Poorer Long-Term Visual Outcomes with Increasing Fluctuating Fluid

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

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

A Post Hoc Analysis of the HAWK and HARRIER Studies



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

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

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

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

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

SOL-1

Post Hoc Analysis: Patients with Retinal Stability at Week 8

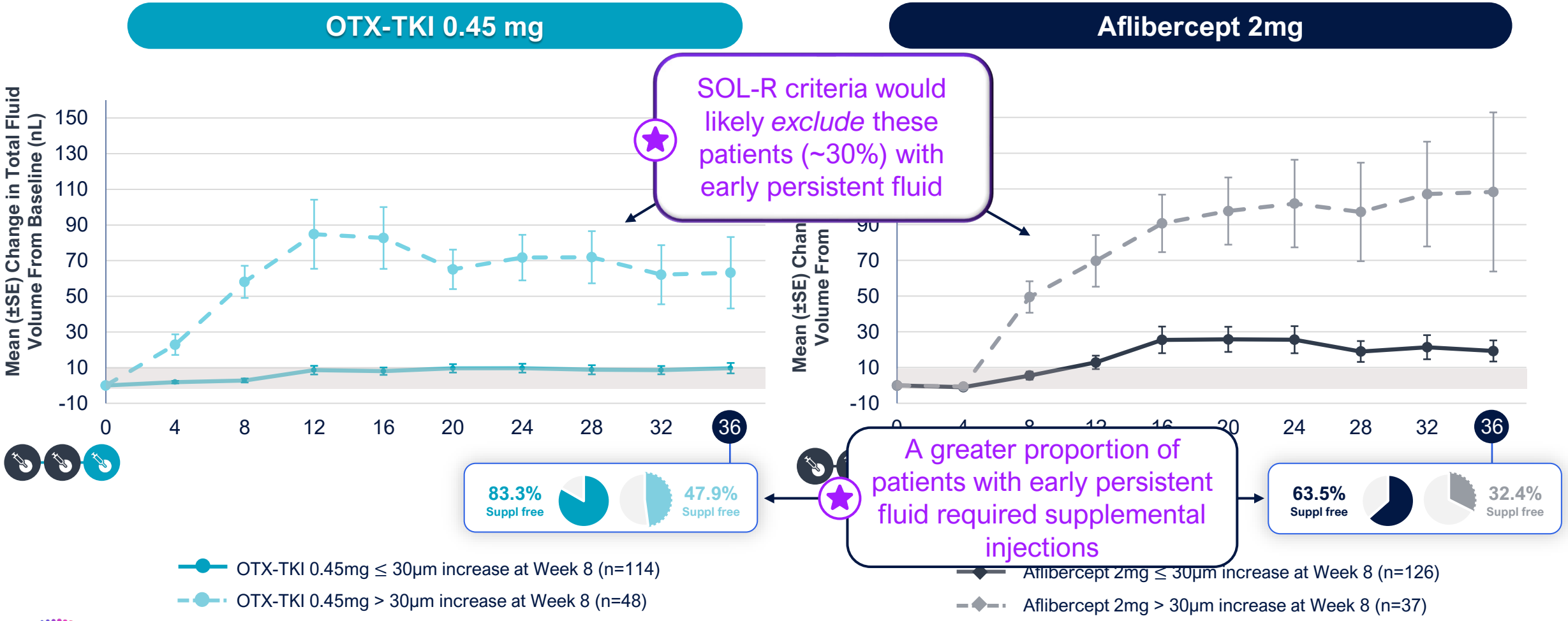
SOL-R criteria would likely *exclude* these patients (~30%) with early persistent fluid

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

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

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

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



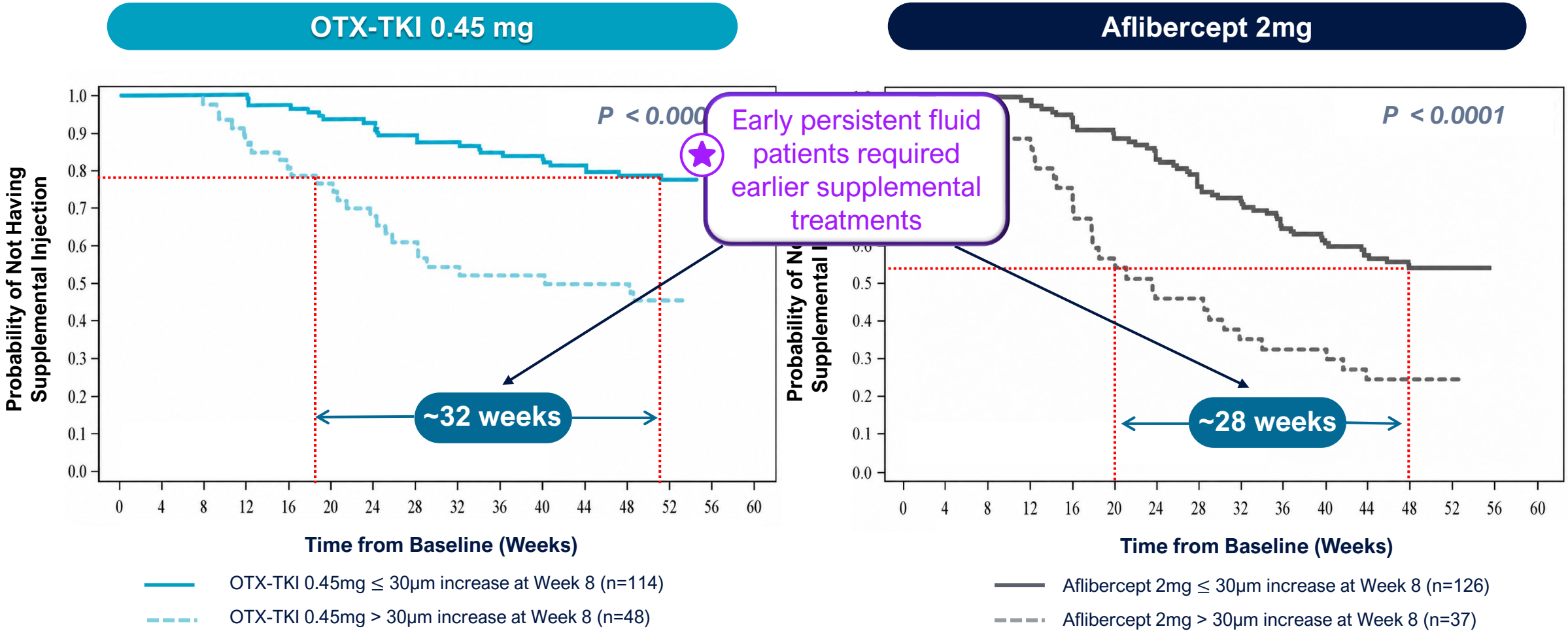
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Retinal stability defined as central subfield thickness ≤30 micron increase on OCT at Week 8. Analyses were based on observed cases; data were missing for 8 subjects in the OTX-TKI arm and 9 in the aflibercept arm at Week 8. For subjects who received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

CSFT, central subfield thickness; Suppl, supplemental; OCT, optical coherence tomography

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

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



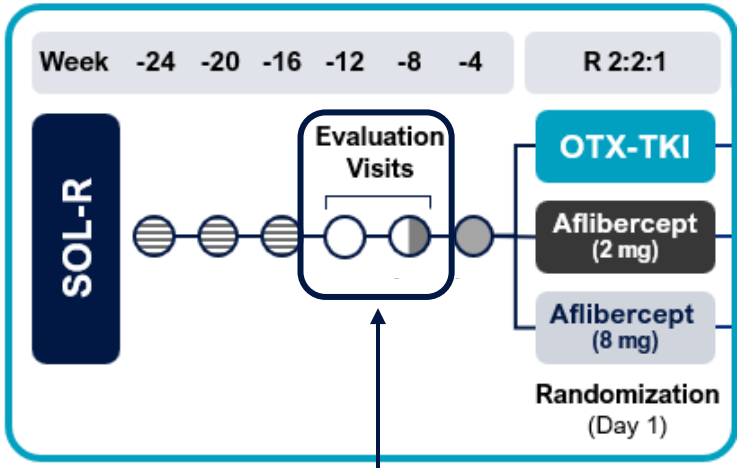
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Core Considerations in nAMD Patient Selection

nAMD Patient Selection

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

SOL-R Screening Period



Two Evaluation Visits

CSFT ≤350 µm at Wk -12 & Wk -8

— AND —

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

Exclude early persistent fluid and fluid fluctuations from SOL-R

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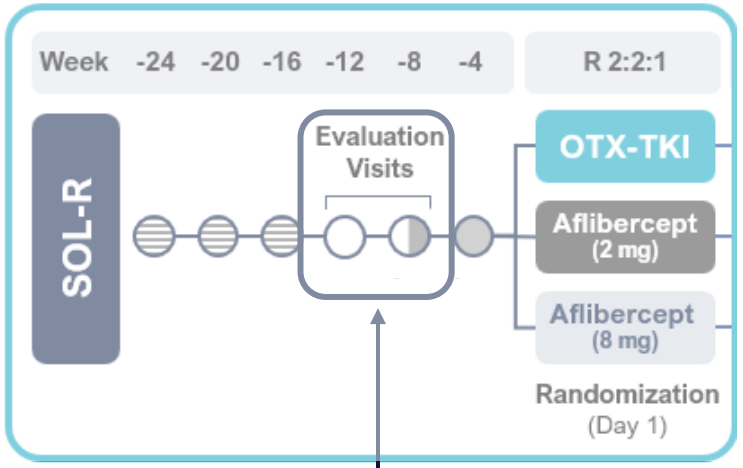
1. Evans RN, et al. *JAMA Ophthalmol*. 2020;138(10):1043-1051; 2. Jaffe GJ, et al. Ophthalmology. 2016;123(9):1856-1864
SF, screen fail; CSFT, central subfield thickness; aVEGF, anti-vascular endothelial growth factor; WK, week

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~20%

Screen fail rate due to early persistent fluid and fluid fluctuations

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

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Key Takeaways

OTX-TKI

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

Axitinib is the most potent retinal TKI in development with 100-fold greater potency against VEGFR-2 relative to vorolanib[2-4]

Durable release for 9-12 months

SOL-1 Clinical Evidence

SOL-1 Phase 3 superiority trial met its primary endpoint

SOL-1 demonstrated superior vision maintenance* versus a single aflibercept 2 mg injection[5]

SOL-R Patient Selection

Patient Selection in Wet AMD is Critical

SOL-R incorporates a 24-week screening period to select patients with demonstrated anti-VEGF response and retinal anatomic stability[6]

Pre-NDA Meeting confirms Ocular's plan to submit OTX-TKI NDA based on SOL-1 Week 52 efficacy and safety, interim SOL-R safety, and confirmatory evidence

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

1. Gross-Goupil M, et al. *Clin Med Insights Oncol*. 2013;7:269-277. 2. Patel C, et al. Target and Selectivity Profiling of Axitinib in Cell-Based and Biochemical Assays. Presented at Association in Vision and Ophthalmology. May 4, 2025. Salt Lake City, UT. 3. Blizzard, C et al. Pharmacodynamic efficacy of optimized intravitreal axitinib implant (OTX-TKI) in a VEGF challenge rabbit model. Presented at the Association in Vision and Ophthalmology. May 9, 2024. Seattle, WA, US. 4. Reaction Biology, Germany; Cellular Phosphorylation Assay Service. (https://www.reactionbiology.com) CHO Cellular assay data demonstrated no TIE2 inhibition within physiological drug solubility range at normal cellular ATP levels via the gold standard cell phosphorylation assay; Ocular Therapeutix. Data on File 042. 2026. 5. Moshfeghi D. Presented at the American Academy of Ophthalmology Retina Subspecialty Day. October 9, 2026. New Orleans, LA. 6. Ocular Therapeutix. Data on File 052.

NDA, new drug application; VEGFR-2, vascular endothelial growth factor receptor 2; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor