# CHANGING THE DME GAMEPLAN WITH FARICIMAB▼

## Dual Pathway, Drying, And Durability

▼ **This medicinal product is subject to additional monitoring.** This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 on the SmPC for information on the reporting of adverse reactions or report to your local Roche Drug Safety contact at: http://www.roche.com/products/local_safety_reporting.htm

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# Welcome & Opening Remarks


## Arshad Khanani (Chair)

Director of Clinical Research, Sierra Eye Associates;
Clinical Professor, University of Nevada, Reno School of Medicine,
Reno, NV, USA

# Disclaimer

**This scientific meeting is sponsored by F. Hoffmann-La Roche Ltd. It is intended for healthcare professionals based in Europe and the US. This program is not affiliated with or endorsed by the ASRS.**

This meeting is intended to facilitate transparent scientific exchange regarding developments in medical research and disease management. The content of this meeting may include scientific information about experimental or investigational compounds, possible indications, and services that are not approved or valid in your country. Providing this scientific information should not be construed as a recommendation to use or prescribe such compounds.

Prescribing information may vary depending on the applicable approval in the respective country. Therefore, before prescribing any product, always refer to applicable local materials such as the prescribing information and/or the Summary of Product Characteristics (SmPC).

**As of July 2024, faricimab is approved for the treatment of neovascular age-related macular degeneration and diabetic macular edema in multiple countries worldwide.**

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reaction. Please report adverse reactions via the https://medinfo.roche.com/ website.

DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration.

# Abbreviated SmPC (Sweden)

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**Composition:** Vabysmo (faricimab) 120 mg/mL solution for injection. Intended for intravitreal use only. Rx, EF, S01LA09.

**Mechanism of action:** Faricimab is a humanised bispecific immunoglobulin G1 (IgG1) antibody that acts through inhibition of two distinct pathways by neutralisation of both angiopoietin-2 (Ang-2) and vascular endothelial growth factor A (VEGF-A).

**Indications:** Faricimab is indicated for neovascular (wet) age-related macular degeneration (nAMD) and visual impairment due to diabetic macular edema (DME).

**Contraindications:** Hypersensitivity to the active substance or to any of the excipients, active or suspected ocular or periocular infections, active intraocular inflammation.

**Warnings:** Endophthalmitis, intraocular inflammation, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract, transient increases in intraocular pressure or intraocular pressure of ≥30 mmHg. Women of childbearing potential should use effective contraception during treatment and for at least 3 months following the last intravitreal injection of faricimab. For complete information, see SmPC at fass.se. Last updated SmPC 2024-02-08.

Date: 02/24 (v2.0).

Ang-2, angiopoietin-2; DME, diabetic macular edema; IgG1, immunoglobulin G1; nAMD, neovascular age-related macular degeneration; SmPC, Summary of Product Characteristics; VEGF-A, vascular endothelial growth factor A.

# Today's Discussions

**Objective**

To demonstrate why **faricimab** could be an important first line treatment to **optimise** outcomes


**How is this achieved?**

**Dual pathway**, **Drying**, and **Durability**

**How do we know this?**

**Clinical trial data** are reflected in the **real-world**

# Expert Panel

**Arshad Khanani (Chair)**

**Director of Clinical Research**

Sierra Eye Associates; Clinical Professor, University of Nevada, Reno School of Medicine, Reno, NV, USA

**Veeral Sheth**

**Partner and Director of Clinical Research**

University Retina and Macula Associates, Chicago, Illinois, USA

**Patricia Udaondo**

**Consultant Ophthalmologist**

Hospital Universitario y Politécnico La Fe
Medical Director, Aiken Clinic
President, Aiken Foundation

**Raj Mukherjee**

**Consultant Ophthalmologist**

Leeds Teaching Hospitals NHS Trust

# Disclosures

## Arshad Khanani (Chair)

- **Consultant:** AbbVie, Adverum, Alcon, Amgen, Annexin, Annexon, Apellis Pharmaceuticals, Aviceda Therapeutics, Beacon Therapeutics, Boehringer Ingelheim, Clearside Biomedical, Complement Therapeutics, 4DMT, Exegenesis, EyePoint Pharmaceuticals, Fronterra Therapeutics, Genentech, Gyroscope Therapeutics, i-Lumen Scientific, Iveric Bio, Janssen Pharmaceuticals, Kodiak Sciences, Kriya Therapeutics, Nanoscope, Novartis, Ocular Therapeutix, Oculis, Ocuphire, OcuTerra, Olive BioPharma, Opthea, Oxular, Oxurion, Perfuse, Ray Therapeutics, Recens Medical, Regeneron Pharmaceuticals, Regenxbio, Revive, RevOpsis, Roche, Sanofi, Stealth BioTherapeutics, Thea Pharma, Unity Biotechnology, Vanotech and Vial
- **Research support:** Aviceda, Adverum, Alexion, Annexon, Apellis Pharmaceuticals, Aviceda Therapeutics, 4DMT, Eyepoint, Exegenesis, Genentech, Gyroscope Therapeutics, Iveric Bio, Janssen, Kodiak, Neurotech, Ocular Therapeutix, Oxular, Regenxbio
- **Stock options:** Aviceda Therapeutics, Oculis, Opthea, PolyPhotonix, Recens Medical, Perfuse, RevOpsis and Vial
- **Board of Directors:** Oculis

## Veeral Sheth

- **Speaker:** Genentech and IvericBio
- **Consultant:** Apellis, EyePoint, Genentech, IvericBio, Kriya Therapeutics, Novartis, Ocular Therapeutix, Ocuphire, Ollin Biosciences, Opthea, Regeneron, RevOpsis, Unity, Vial
- **Contracted research:** 4D Molecular Therapeutics, Abbvie, Adverum Biotechnologies, Alimera Sciences, Ashvattha Therapeutics, Aviceda, Chengdu Kanghong, Eyebiotech, Eyepoint Pharmaceuticals, Genentech, Gyroscope Therapeutics, i-Lumen Scientific, Ionis, IvericBio, Janssen Pharmaceuticals, NGM Biopharmaceuticals, Novartis, Ocular Therapeutix, Ocugen, OcuTerra, Olix, Opthea, Outlook, Oxular, Oxurion, Perfuse Therapeutics, Recens Medical, Regeneron Pharmaceuticals, RegenXBio, Rezolute, Roche, SalutarisMD, SamChungDang, Santen, Smilebiotek, Unity Biotechnology, Vanotech

## Patricia Udaondo

- **Consultant:** AbbVie, Alimera, Apellis, Bayer, Boehringer-Ingelheim, Brill pharma, EyePoint, Ocular Therapeutix, Ocuphire, OcuTerra, Outlook Therpaeutics, Roche.
- **Lecture Fees:** AbbVie, Alimera, Apellis, Bayer, Brill pharma, Bausch-Lomb, Roche

## Raj Mukherjee

- **Consultant:** Abbvie, Alimera, Bayer, Janssen, Nordic, Novartis, Roche
- **Research support:** Bayer, Chengdu Kanghong, Janssen, Novartis, Oxurion, Roche, Stealth

# Agenda

**Faricimab: The Landscape So Far**

Arshad Khanani (Chair)

**Dual Pathway**

**The Difference With Dual Pathway Inhibition**

Patricia Udaondo

**Drying**

**Achieving Disease Control**

Veeral Sheth

**Durability**

**Reducing Treatment Burden**

Raj Mukherjee

**Closing Remarks**

Arshad Khanani (Chair)

# Gameshow Instructions

## Roles and Course of Play

1. Chair is the gameshow host
2. Speakers are the contestants
3. Contestants will be asked a question at the end of each section, but they may need your expertise!

## Lifelines

**Phone a friend**

Allows the contestant to ask another contestant their opinion

**Ask the Audience**

Audience vote via a show of hands to assist the contestant


**50/50**

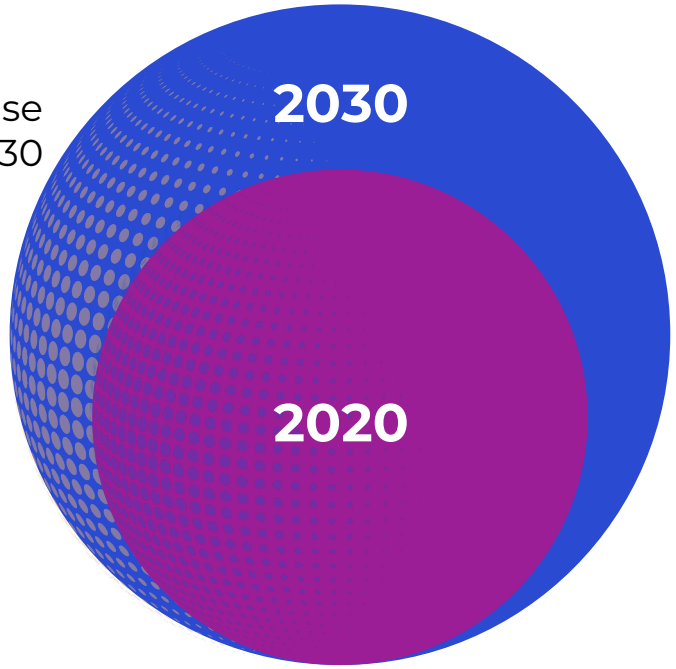
Removes two of the wrong answers

# Faricimab: The Landscape So Far

# While Anti-VEGFs Have Redefined Patient Care, They Do Not Address The Multifactorial Nature Of DME[1]

**25%**

expected increase from 2020 to 2030 in the global prevalence of DME[2]




## Unmet needs in DME remain

- Frequent injections[3,4]
- Patient and caregiver burden[4,5]
- Missed clinic visits[6,7]
- Suboptimal long-term outcomes[3]

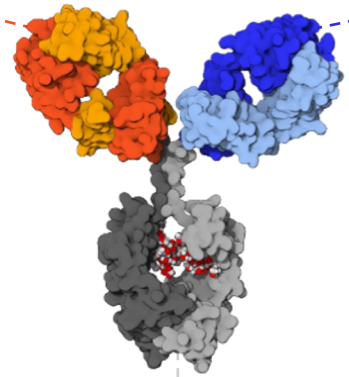
With the increased demand on healthcare services due to this increased prevalence, more durable treatments that reduce treatment burden will help to free up capacity[2]

DME, diabetic macular edema, VEGF, vascular endothelial growth factor. 1. Liberski S *et al.* Int J Mol Sci. 2022;23(16):9424; 2. Tan T-E and Wong TY. Front Endocrinol. 2023;13:1077669; 3. Ciulla TA, *et al.* Br J Ophthalmol. 2021;105:216–221; 4. Sivraprasad S, *et al.* Clin Ophthalmol. 2016;10:939–946; 5. Spooner KL, *et al.* Diabetes Metab Syndr Obes. 2019;12:1913–1921; 6. Kiss S, *et al.* Clin Ophthalmol. 2016;10:2443–2453; 7. Sheth V, *et al.* Invet Ophthalmol Vis Sci. 2022;63:4205–A0133.

# Faricimab: One Molecule With Two Signaling Pathway Targets For Durable Efficacy[1-3]

## Anti–Ang-2 Fab

**Stabilises vessels[3]**
**Reduces vascular leakage[3]**
**Reduces inflammation[3]**



## Anti–VEGF-A Fab

**Reduces vascular leakage[3]**
**Inhibits neovascularisation[3]**

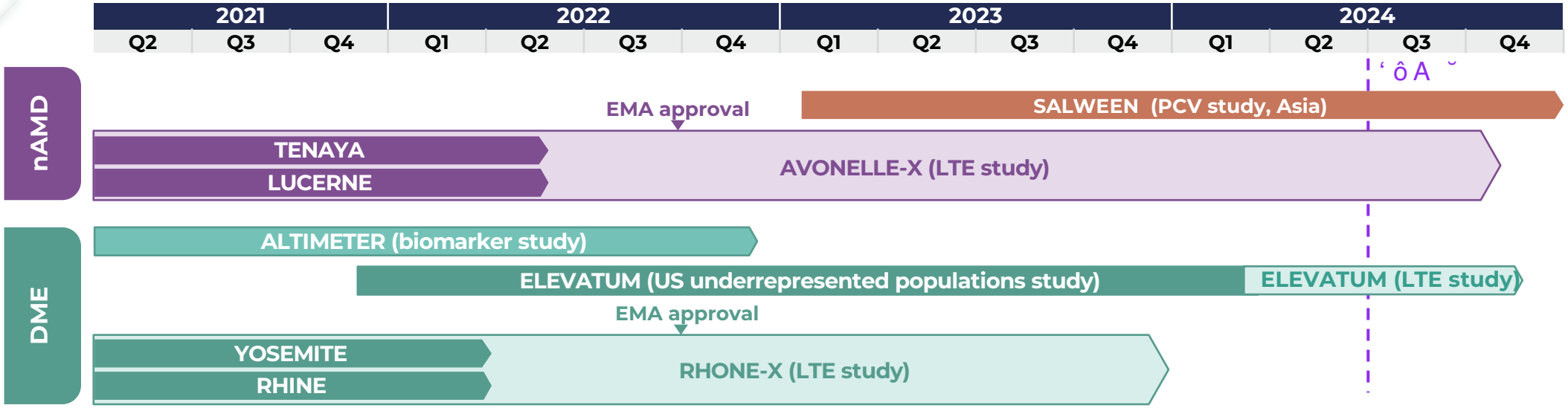
## Modified Fc

**Reduces systemic exposure[3]**
**Reduces inflammatory potential[3]**

Adapted from Sahni J *et al.* Ophthalmology. 2019;126(8):1155–1170.

CrossMAb molecule representative of faricimab. Faricimab molecule image reprinted from Sahni J *et al.* Ophthalmology. 2019;126(8):1155–1170, Copyright (2019), with permission from the American Academy of Ophthalmology.[2]
Ang-2, angiopoietin 2; Fab, fragment antigen binding; Fc, fragment crystallisable; VEGF-A, vascular endothelial growth factor A. 1. Panos GD *et al.* Drug Des Dev Ther. 2023;17:2861–2873; 2. Sahni J *et al.* JAMA Ophthalmology. 2020;138(9):955–963; 3. Regula JT *et al.* EMBO Mol Med. 2016;8:1265–1288.

# Faricimab Has An Extensive And Ongoing Clinical Development Program




**YOSEMITE & RHINE: The largest Phase 3 registrational trials in DME[1]**

**RHONE-X: A long-term extension study with 2-years additional follow-up[2]**

**1,891** patients

4 years total follow-up

**1,474** patients

DME, diabetic macular edema; EMA, European Medicines Agency; LTE, long-term extension; nAMD, neovascular age-related macular degeneration; PCV, polypoidal choroidal vasculopathy; Q, quarter. 1. Wykoff CC *et al.* Lancet. 2022;399:741–755; 2. Khanani A *et al.* ASRS 2024. ALTIMETER clinical trial (NCT04597918); AVONELLE-X clinical trial (NCT04777201); ELEVATUM clinical trial (NCT05224102); LUCERNE clinical trial (NCT03823300); RHINE clinical trial (NCT03622593); RHONE-X clinical trial (NCT04432831); SALWEEN clinical trial (ISRCTN69073386); TENAYA clinical trial (NCT03823287); YOSEMITE clinical trial (NCT03622580).

# Faricimab Is Supported By A Real-World Data Program Of >100,000 Patients

## Roche-sponsored studies[1–6]

- VOYAGER
- FARETINA-nAMD (IRIS® registry)
- FARETINA-DME (IRIS® registry)
- FARWIDE-nAMD (Medisoft EMR)
- FARWIDE-DME (Medisoft EMR)
- PASSENGER

**6 ongoing real-world studies**

**>100,000 patients projected for nAMD and DME**

**28 countries**

## Independent data[7–17]

**Over 50 independent publications in >2,500 patients including:**

- Cheng et al.
- Khanani et al.
- Kusuhara et al.
- Leung et al.
- Matsumoto et al.
- Mukai et al.
- Ohara et al.
- Rush and Rush
- Stanga et al.
- Grimaldi et al.

Faricimab has demonstrated **favourable efficacy** in real-world studies, and presented **no new safety concerns**

DME, diabetic macular edema; EMR, electronic medical records; IRIS, Intelligent Research in Sight; nAMD, neovascular age-related macular degeneration. 1. VOYAGER clinical trial (NCT05476926); 2. Tabano D *et al.* ARVO 2024; 3. Borkar D *et al.* ARVO 2024; 4. Varma D *et al.* ARVO 2024; 5. Reynolds R *et al.* ARVO 2024; 6. Paul-Ehrlich-Institut. https://www.pei.de/SharedDocs/awb/nis-0701-0800/0711.html [last accessed May 2024]; 7. Cheng AM *et al.* Cureus. 2023;15(6):e40100; 8. Khanani AM *et al.* Eye. 2023;37:3574–3581; 9. Kusuhara S *et al.* Medicina (Kaunas). 2023;59:665; 10. Leung EH *et al.* Clin Ophthalmol. 2023;17:1287–1293; 11. Matsumoto H *et al.* Graefes Arch Clin Exp Ophthalmol. 2023;261:2945–2952; 12. Mukai R *et al.* Sci Rep. 2023;13:8747; 13. Ohara H *et al.* Medicina. 2023;59:1125; 14. Rush RB and Rush SW. Clin Ophthalmol. 2022;16:2797–2801; 15. Rush RB and Rush SW. Clin Ophthalmol. 2022;16:4041–4046; 16. Stanga PE *et al.* Eye. 2023;37:3282–3289; 17. Grimaldi G *et al.* Graefes Arch. 2024;262(4):1151–1159.

# Dual Pathway: The Difference With Dual Pathway Inhibition


Patricia Udaondo

Consultant Ophthalmologist, Hospital Universitario y Politécnico La Fe

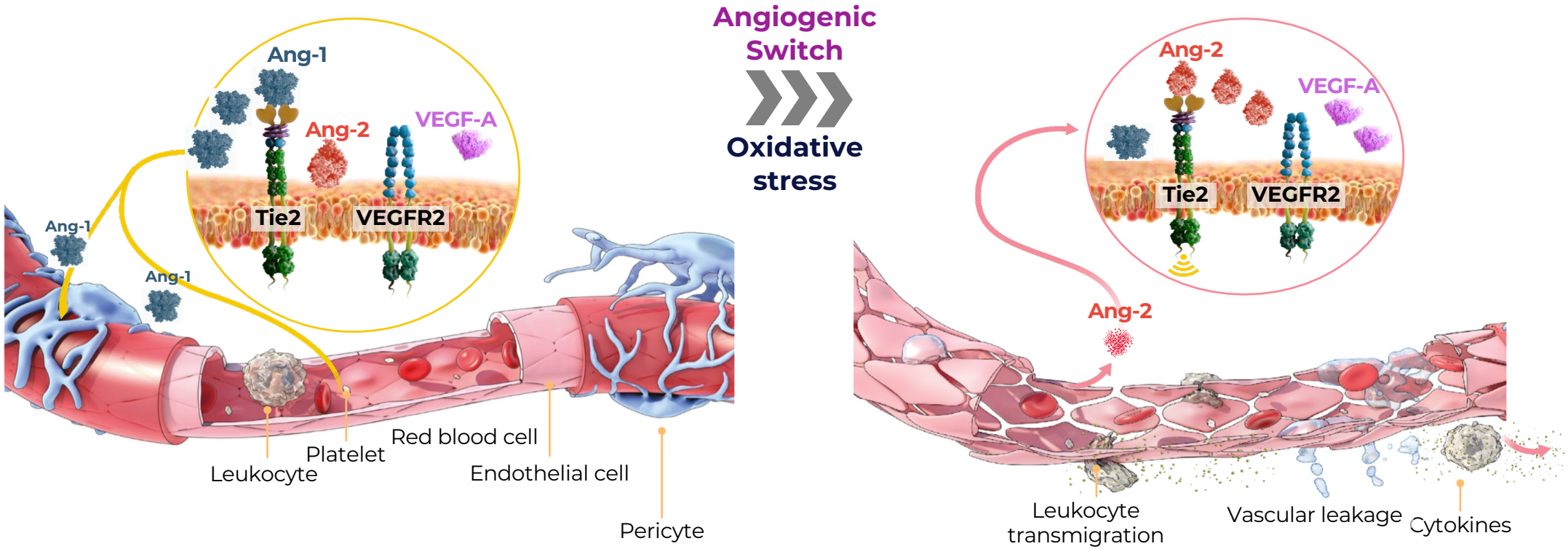
Medical Director, Aiken Clinic

President, Aiken Foundation

# Elevated Ang-2 Contributes To Vascular Instability[1–4]

**↓ Ang-2 »** **Vascular STABILITY In Healthy Tissues**

**↑ Ang-2 »** **Drives Vascular INSTABILITY In Pathologic Tissues**




Adapted from The Angiogenesis Foundation Infographic.

Ang-1, angiopoietin-1; Ang-2, angiopoietin-2; Tie2, tyrosine kinase with immunoglobulin-like domains-2; VEGF-A, vascular endothelial growth factor-A; VEGFR2, vascular endothelial growth factor receptor-2.

1. Saharinen P et al. Nat Rev Drug Discov. 2017;16(9):635–661; 2. Nambu H et al. Gene Ther. 2004;11(10):865–873; 3. Mueller SB, Kontos CD. J Clin Invest. 2016;126(9):3188–3191;
4. The Angiogenesis Foundation. https://www.scienceofang2.org/. Accessed June 2024.

# In DME, Multiple Clinical Biomarkers Provide Evidence For The Benefit Of Dual Pathway Compared To VEGF Inhibition Alone

**Dual pathway inhibition with faricimab: Anti–Ang-2 + Anti–VEGF-A[1]**

## Elevated VEGF[2]

### Neovascularization[5,6]

Reduction of **fluid on OCT**[14,15]

### Vascular leakage[7]

Reduction of **fluid on OCT**[14,15]

Resolution of **macular leakage**[18]
Reduction of **hard exudates**[19]

## Elevated Ang-2[1,3,4]

### Vascular leakage[7]

Reduction of **fluid on OCT**[14,15]

Resolution of **macular leakage**[18]
Reduction of **hard exudates**[19]

### Inflammation[5,6,8]

Reduction of **HRF**[16]

### Fibrosis[9-13]

Reduction of **ERM** development[17]

**Disease control with faricimab vs anti-VEGF monotherapy[14-20]**

**Extended durability beyond Q12W[20-22]**

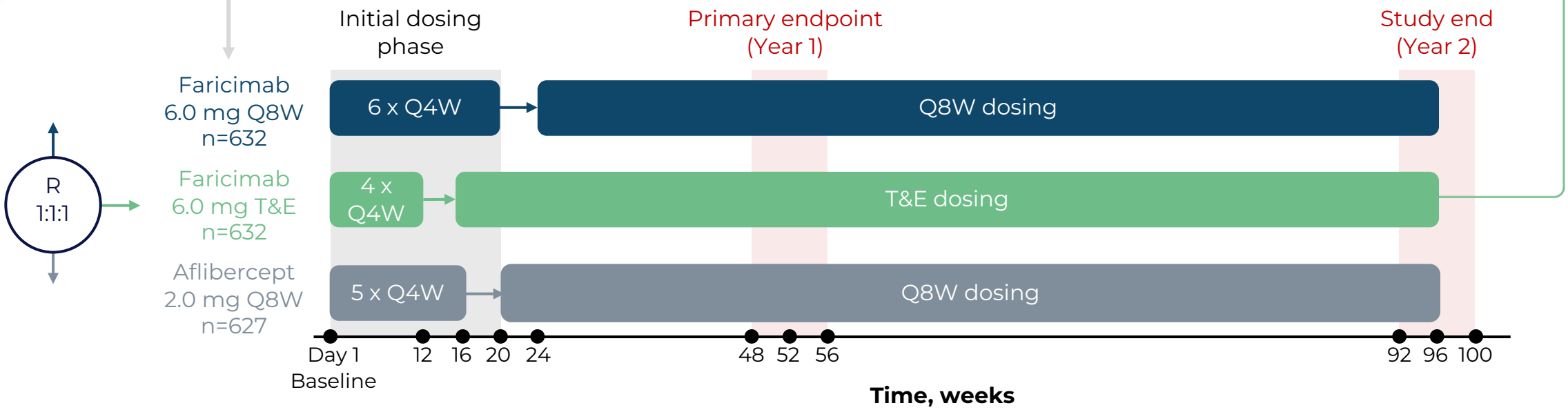
VEGF | VEGF & Ang-2 | Ang-2

Ang-2, angiopoietin-2; DME, diabetic macular edema; ERM, epiretinal membrane; HRF, hyperreflective foci; OCT, optical coherence tomography; QXW, every X weeks; VEGF, vascular endothelial growth factor; VEGF-A, vascular endothelial growth factor-A. 1. Regula JT *et al.* EMBO Mol Med. 2016;8:1265–1288; 2. Aiello LP *et al.* N Engl J Med. 1994;331:1480–1487; 3. Tsai T *et al.* PLoS One. 2023;18:e0280488; 4. Ng D *et al.* Sci Rep. 2017;7:45081; 5. Kim S-Y *et al.* Ann Eye Sci. 2021;6:24; 6. Collazos-Aleman JD *et al.* Diabetes Ther. 2022;13:1811-1821; 7. Rangasamy S *et al.* Invest Ophth Vis Sci. 2011;52(6):3784-3791; 8. Hirasawa M *et al.* J Biol Chem. 2016;291:7373–7385; 9. Larsen OH *et al.* Ophth Ther. 2023;12:2253–2264; 10. Canonica J *et al.* Front Cell Neurosci. 2023;17:1192464; 11. Klaassen I *et al.* PLoS One. 2017;12:e0187304; 12. Takagi H *et al.* Invest Ophth Vis Sci. 2003;44:393–402; 13. Umeda N *et al.* Ophthalmic Res. 2003;35:217–223; 14. Pollreisz A *et al.* Invest Ophthalmol Vis Sci. 2023;64(8):2817; 15. Querques G *et al.* Invest Ophthalmol Vis Sci. 2023;64:2185; 16. Maunz A *et al.* Invest Ophthalmol Vis Sci. 2023;64:PB0039; 17. Jaffe G *et al.* ASRS 2023; 18. Goldberg RA *et al.* Invest Ophthalmol Vis Sci. 2023;64:2816; 19. Goldberg *et al.* ARVO 2024; 20. Wong TY *et al.* Ophthalmology. 2024;131(6):708-723; 21. Lim JI *et al.* Invest Ophthalmol Vis Sci. 2023;64:2185; 22. Lim JI. Angiogenesis, Exudation, and Degeneration 2024 Virtual Congress.

# Faricimab DME Trials Use Disease Criteria Reflective Of Clinical Practice[1]

Naïve or previously treated patients[a] (1 eye per patient)
- Center-involving DME (**CST ≥325 µm**)[b]
- **BCVA 25–73 ETDRS letters** (Snellen ~20/320–20/40)[c]

Extend by 4 weeks up to Q16W, if stable CST and BCVA
Reduce by 4 or 8 weeks as low as Q4W, if worsening CST +/- BCVA
Maintain dosing interval if extension or reduction criteria not met



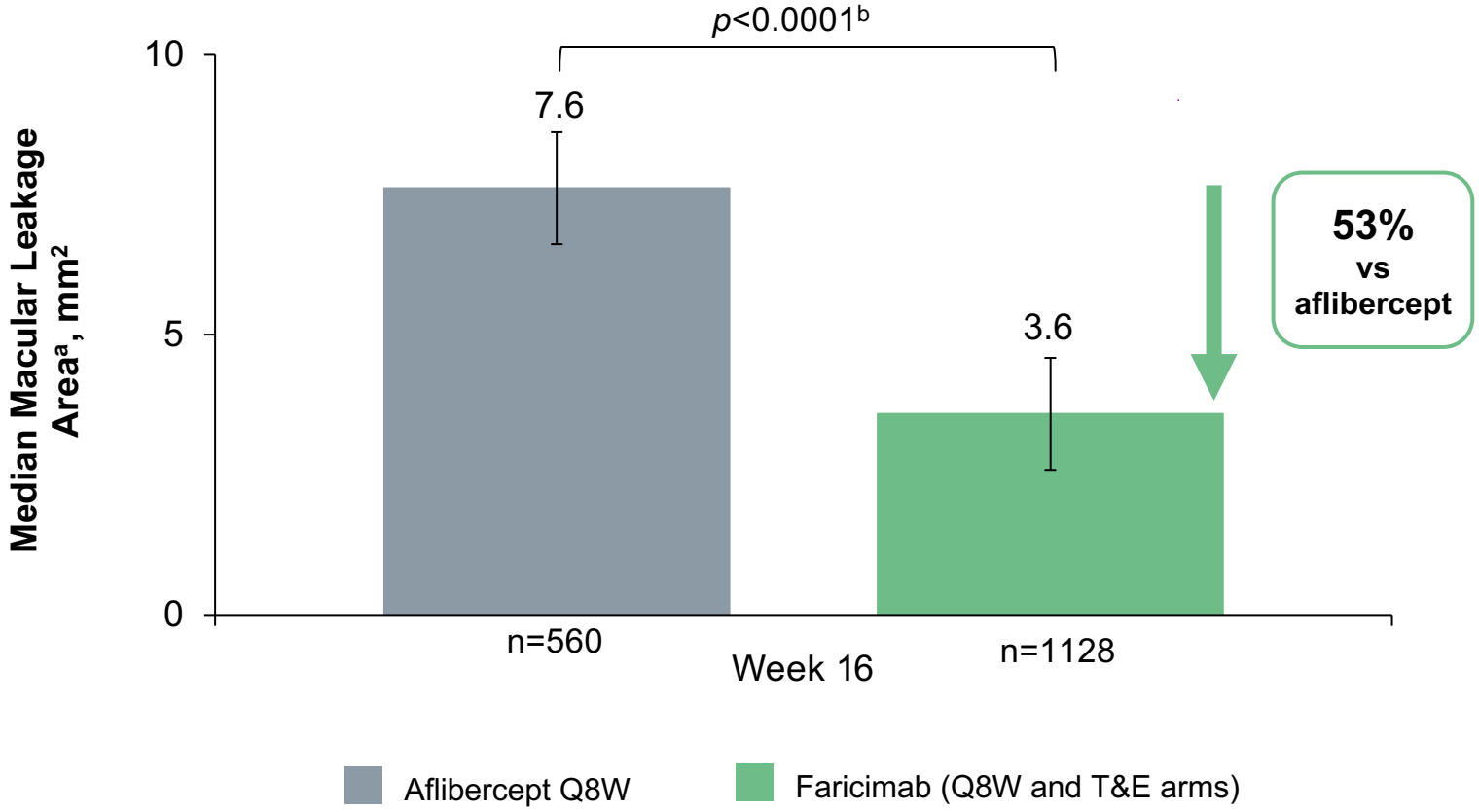

Adapted from Talcott K *et al.* Hawaiian Eye and Retina 2024.

Patients in all arms were required to attend study visits every 4 weeks and received a sham procedure at non-active dosing visits to preserve treatment masking. Week 100 was a non-dosing visit. [a]Previously anti-VEGF–treated eyes (treated ≥ 3 months before Day 1) were limited to 25% of the total enrollment. [b]CST was measured as the distance from the ILM to Bruch's membrane. [c]BCVA was measured using the ETDRS VA chart at a starting distance of 4 m. BCVA, best corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; ILM, internal limiting membrane; QXW, every X weeks; R, randomization; T&E, treat-and-extend; VA, visual acuity; VEGF, vascular endothelial growth factor. 1. Talcott K *et al.* Hawaiian Eye and Retina 2024 Meeting.

# Greater Reduction In Macular Leakage Area With Faricimab Vs Aflibercept[1]

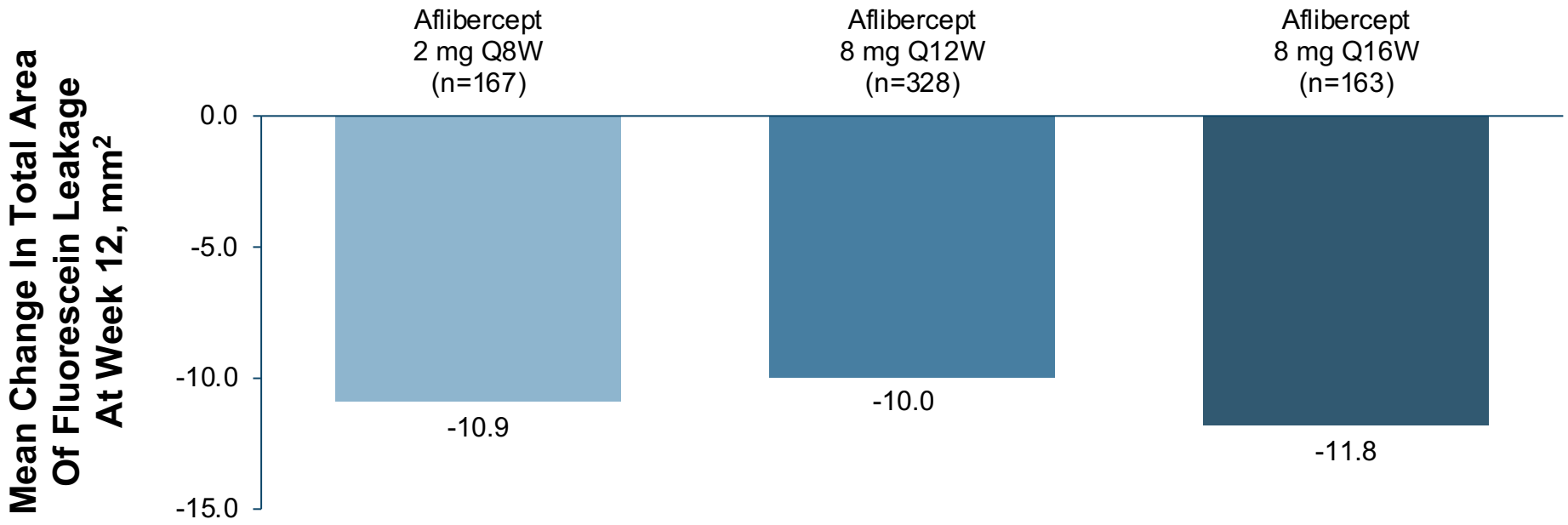
## YOSEMITE/RHINE pooled post hoc analysis

Head-to-head dosing phase (Week 16)




[a]Macular leakage area determined by fluorescein angiography. [b]The p value from Wilcoxon 2-sample rank test is nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the p values. 95% CIs are shown. CI, confidence interval; QXW, every X weeks; T&E, treat-and-extend. 1. Sivaprasad S *et al.* EURETINA 2023.

# PHOTON: Increasing The Dose Of Aflibercept By 4 Times Did Not Improve Macular Leakage Area[1]

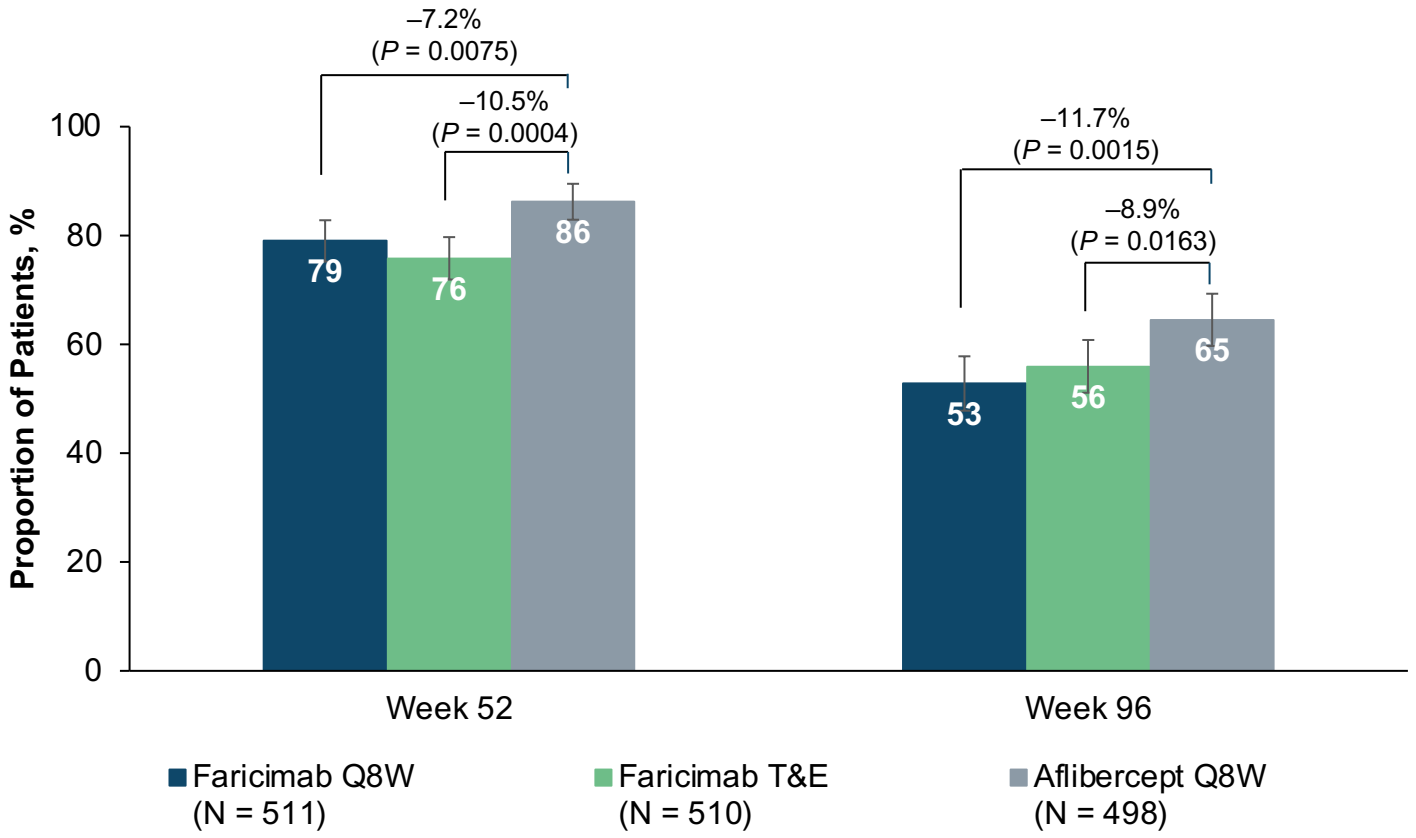



QXW, every X weeks. PHOTON (NCT04429503.) 1. Sivaprasad S *et al.* EURETINA 2023.

# Fewer Patients With Hard Exudates At Weeks 52 and 96 With Faricimab Vs Aflibercept[1]

## YOSEMITE/RHINE pooled post hoc analysis

Patients with hard exudates at baseline (81% of patients in the study)

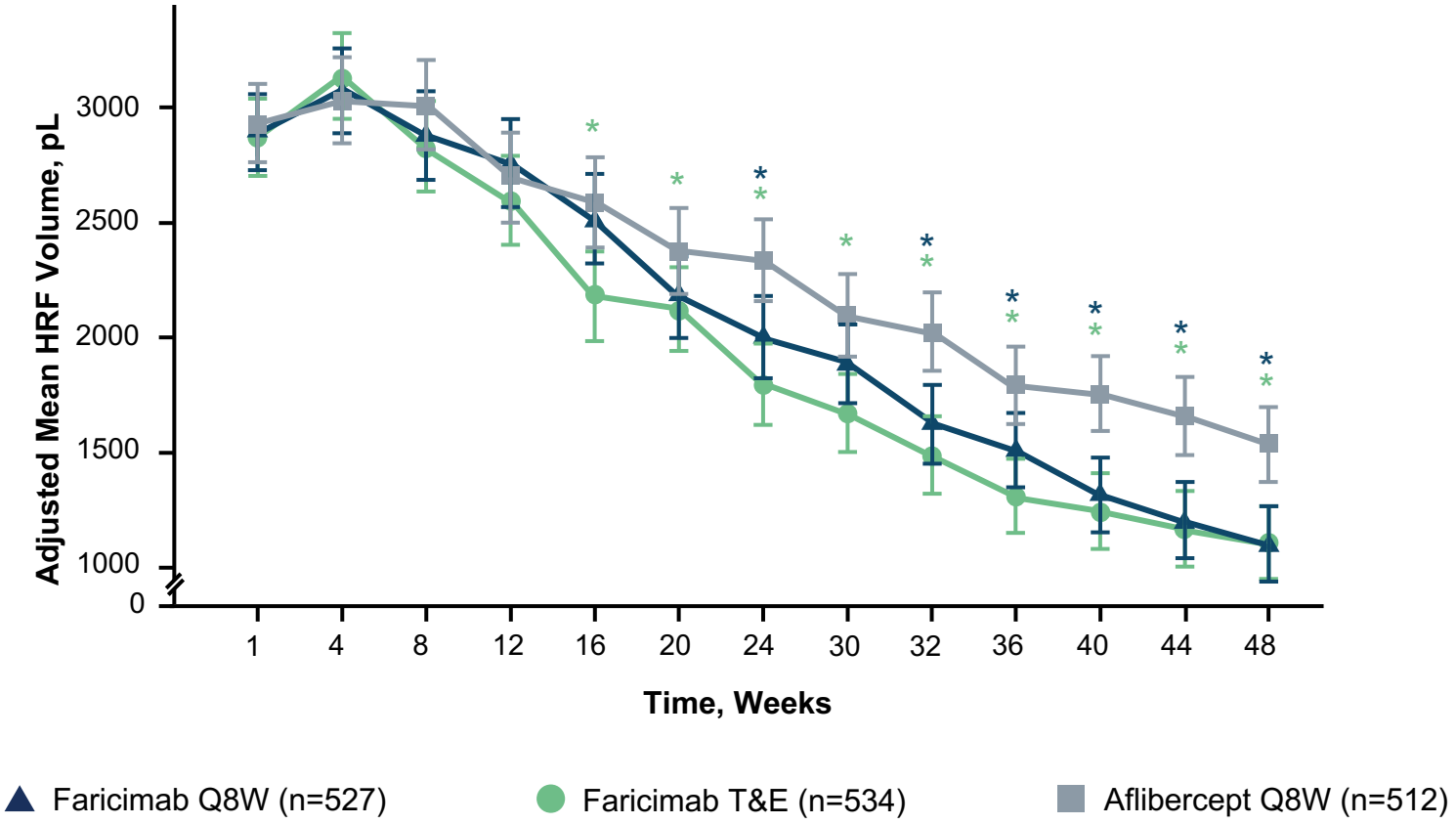



Analysis based on patients with HE at baseline. HE was evaluated at a Central Reading Center using color fundus photography. The weighted estimate is based on Cochran-Mantel-Haenszel test stratified by baseline BCVA score (<64 letters vs ≥64 letters), prior Intravitreal anti-VEGF therapy (yes vs no), region (US and Canada vs the rest of the world), and study (YOSEMITE vs RHINE). Missing data were not imputed. 95% CI is reported. Estimates below 0% or above 100% are imputed as 0% or 100%, respectively. Baseline is defined as the last available measurement obtained on or before randomization. Presence of HEs is defined as HEs within ETDRS Grid equal to Definite or Questionable. Absence of HEs is defined as HEs within ETDRS Grid equal to Absent. The p values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the p values. BCVA, best-corrected visual acuity; CI, confidence interval; ETDRS, Early Treatment Diabetic Retinopathy Study; HE, hard exudates; QXW, every X weeks; T&E, treat-and-extend; VEGF, vascular endothelial growth factor. 1. Lim JI *et al.* CTS Annual Meeting 2024.

# Greater Reduction In HRF Volume Observed With Faricimab Vs Aflibercept[1]

## YOSEMITE/RHINE pooled post hoc analysis

Volume in the total retina[a] (3 mm diameter)

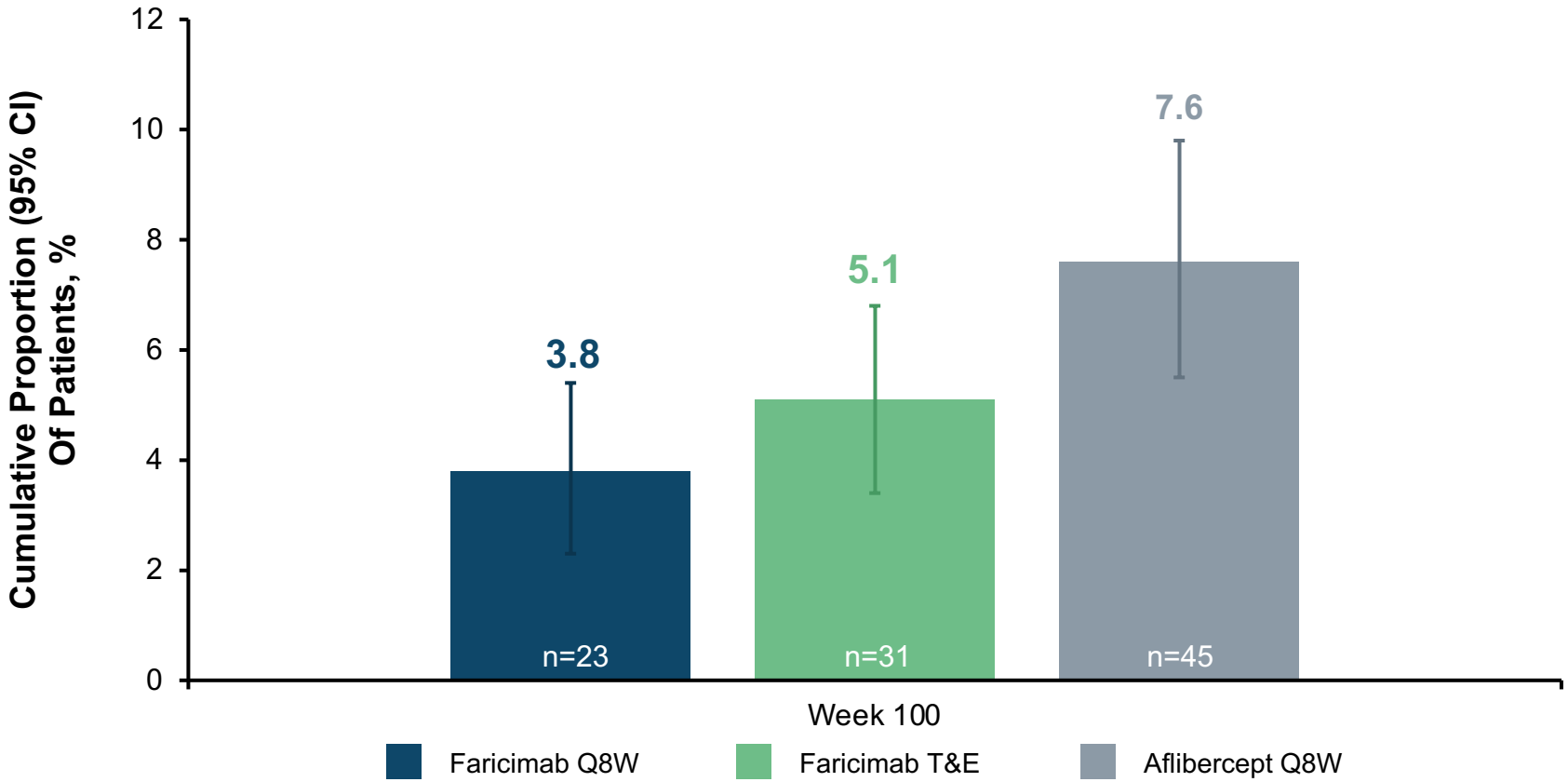



[a]ILM to RPE. Results are based on a mixed model for repeated measures adjusted for baseline HRF result, treatment arm, visit, visit-by-treatment arm interaction, baseline BCVA, baseline BCVA category (<64 letters vs ≥64 letters), region (US and Canada, Asia and the rest of the world) and prior intravitreal anti-VEGF therapy (yes vs no). An unstructured covariance structure was used. 95% CI error bars are shown. MMRM analyses performed on original units (μm3) but axis values converted to pL for mean plots. *P values are nominal and not adjusted for multiplicity (nominal p value <0.05 vs aflibercept 2 mg Q8W); no formal statistical conclusion should be made based on the p values.
BCVA, best-corrected visual acuity; CI, confidence interval; HRF, hyperreflective foci; ILM, internal limiting membrane; MMRM, mixed model repeated measures; QXW, every X weeks; RPE, retinal pigmented epithelium; T&E, treat-and-extend; VEGF, vascular endothelial growth factor. 1. Graff J,*et al.* Hawaiian Eye and Retina Meeting 2024.

# Lower Risk Of ERM Formation With Faricimab Vs Aflibercept[1]

## YOSEMITE/RHINE pooled post hoc analysis

Cumulative proportion of patients who developed an ERM during the study (%)[a]




**At Week 100**
**Faricimab Q8W**
**vs Aflibercept Q8W**

Odds Ratio[b]: **0.48**
95% CI: **0.29, 0.81**
*P* value: **0.0055**

**At Week 100**
**Faricimab T&E**
**vs Aflibercept Q8W**

Odds Ratio[b]: **0.65**
95% CI: **0.41, 1.05**
*P* value: **0.0783**

Eyes with no ERM at baseline. Missing data were not imputed, and eyes with no postbaseline ERM results were excluded from the analysis. ERMs defined as presence of significant distortion of macular architecture in the central subfield. [a]The denominator is the number of eyes with no ERMs at baseline who had ERM status available through the study. Once an individual was noted to have an ERM, they were accounted for in the numerator with the assumption that ERMs remain present. [b]The adjusted odds ratio and 95% CI were produced using a multivariate logistic regression models including treatment group, baseline BCVA score (< 64 letters vs ≥ 64 letters), prior IVT anti-VEGF therapy (yes vs no), region (US and Canada, and the rest of the world), and study (YOSEMITE vs RHINE) as covariates using cumulative data through week 100. Risk refers to the odds from logistic regression. The P values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the P values. BCVA, best-corrected visual acuity; CI, confidence interval; ERM, epiretinal membrane; IVT, intravitreal therapy; QXW, every X weeks; T&E, treat-and-extend; VEGF, vascular endothelial growth factor. 1. Udaondo P *et al.* Retina World Congress 2024.

# Summary of Experience with Faricimab

**Started treating** DME patients with faricimab in **December 2023**

Treated **36 DME** eyes (80% refractory; 20% treatment-naïve)

Switch eyes respond better if **loaded** before extending

Treatment-naïve eyes respond **better and faster**

For the **cohort** of eyes treated so far:
**Baseline BCVA: 61 +/- 7 letters**
**After 6 months follow-up: 69 +/- 8 letters**

BCVA, best-corrected visual acuity; DME, diabetic macular edema.

# Case 1

| Patient History | |
|---|---|
| **Age** | 66 |
| **Sex** | Female |
| **Disease** | DME |
| **Disease Duration** | 2 years |
| **Affected Eye(s)** | Both eyes |
| **Ocular History** | No ocular history |
| **Patient Background** | Type 2 diabetes, obese, hypertension, pseudophakic |

**Right Eye**

**Baseline BCVA:**
20/50

**Left Eye**

**Baseline BCVA:**
20/40

**Diagnosed With DME:**
2022

**Bilateral treatment history**

July 2022: Aflibercept 2 mg – slow responder

December 2022: Dexamethasone implant – intraocular pressure increased

March 2023: Aflibercept 2 mg

BCVA, best-corrected visual acuity; DME, diabetic macular edema.

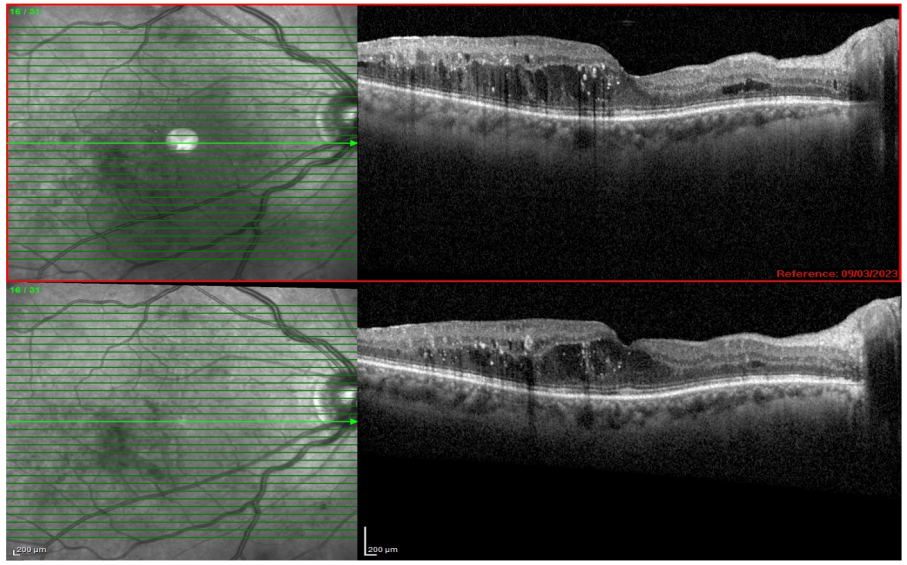
# Case Study: DME In Both Eyes Treated With Faricimab Q4W

**Right Eye**

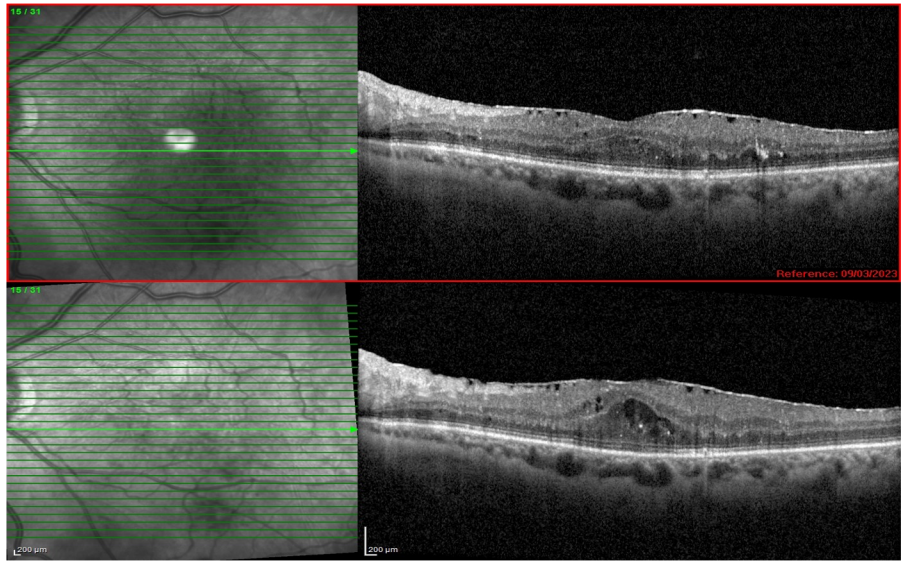
**Left Eye**

**After 5x Aflibercept Injections**
January 2024

**BCVA:** 20/50



**BCVA:** 20/40



Faricimab #1 given

**Faricimab**

#1

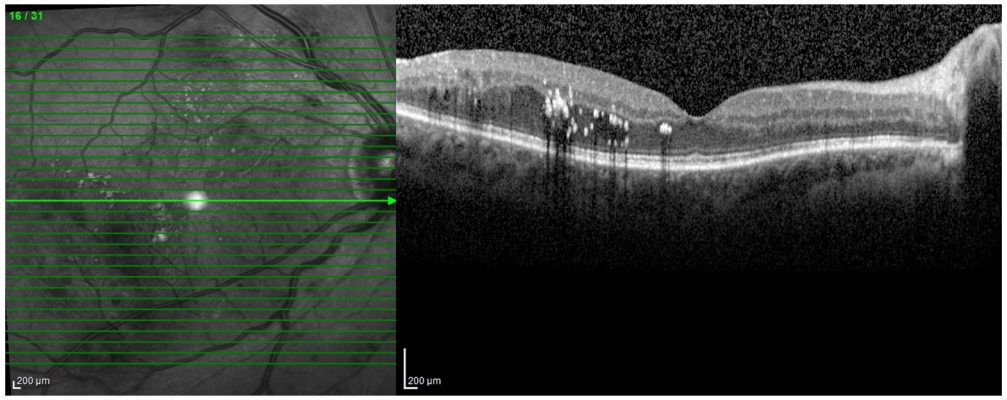
BCVA, best-corrected visual acuity; DME, diabetic macular edema; QXW, every X weeks.

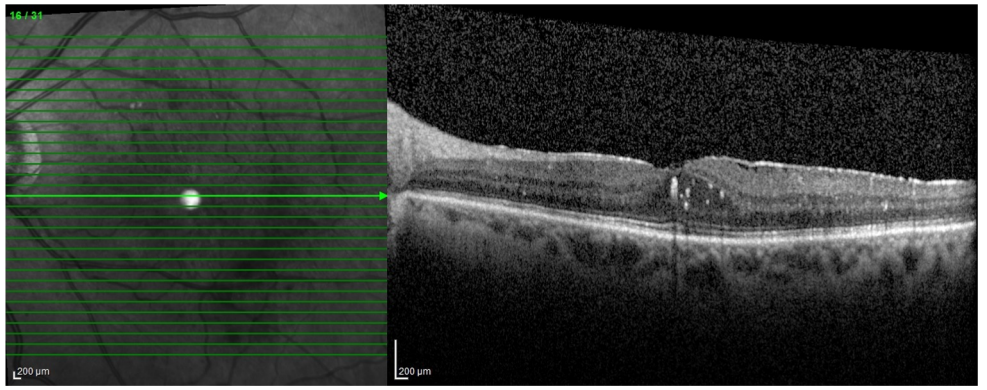
# Case Study: DME In Both Eyes Treated With Faricimab Q4W

**Right Eye**

**Left Eye**

**4 Weeks After Faricimab #3**
April 2024




**Faricimab #4 given**

**Faricimab**

#1 Q4W #2 Q4W #3 Q4W #4

DME, diabetic macular edema; QXW, every X weeks.

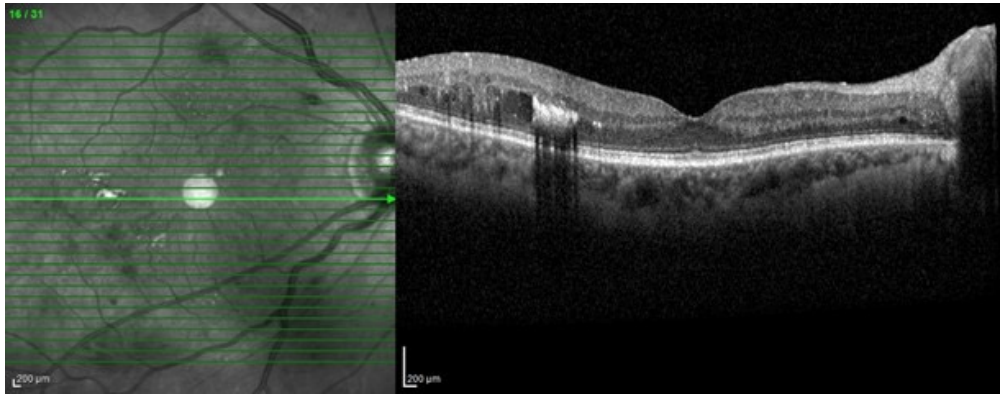
# Case Study: Extended From Faricimab Q4W To Q8W

**Right Eye**

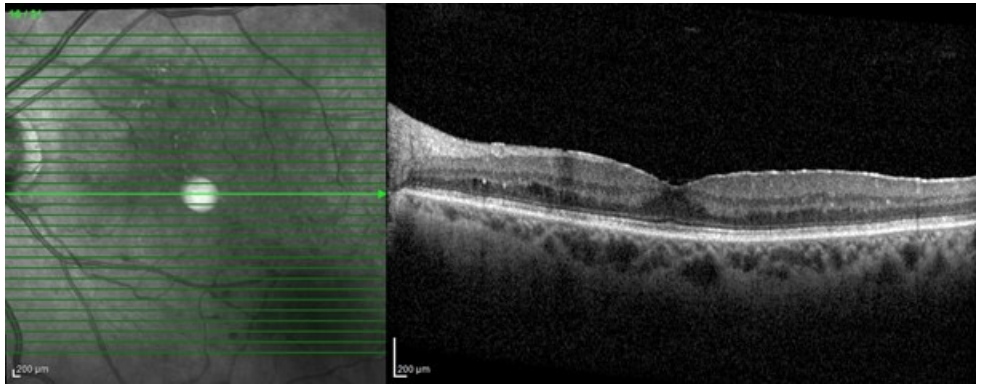
**Left Eye**

**8 Weeks After Faricimab #4**
June 2024

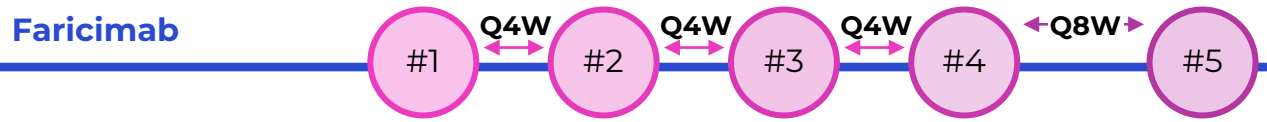
**BCVA:** 20/25



**BCVA:** 20/20



Faricimab #5 given




BCVA, best-corrected visual acuity; DME, diabetic macular edema; QXW, every X weeks.

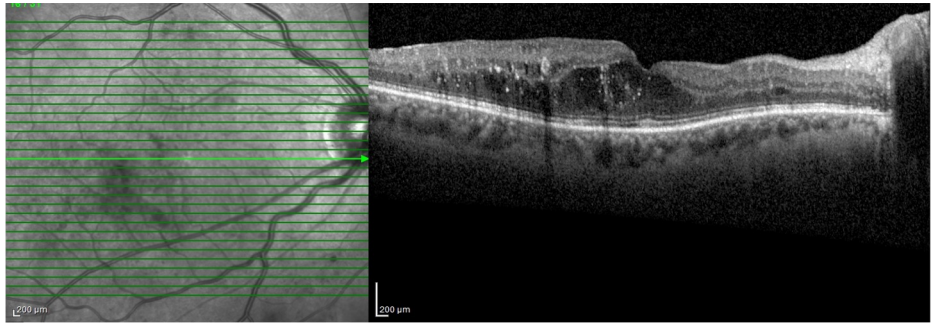
# Case Study: Summary And Discussion

**Right Eye**

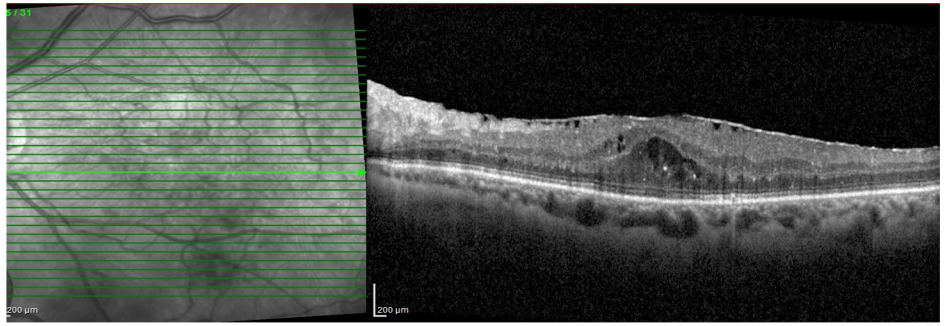
**After dexamethasone implant and aflibercept injections**

**Left Eye**

**BCVA:** 20/50

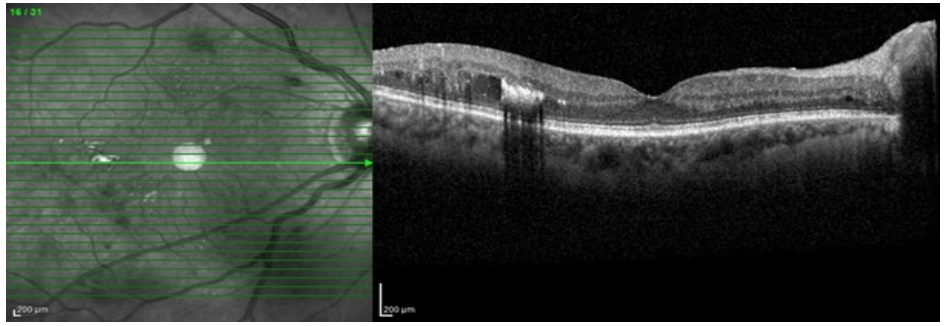


**BCVA:** 20/40

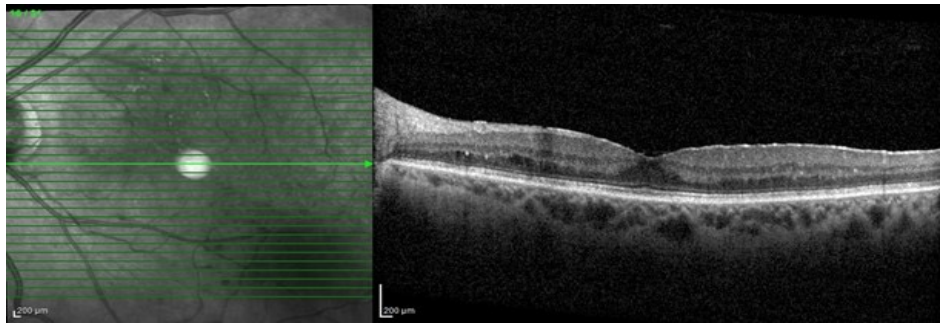


**BCVA:** 20/25

**After 4x Q4W faricimab**



**BCVA:** 20/20



Previous treatment: Good response to steroids but intraocular pressure increased; incomplete response to anti-VEGF

Faricimab treatment: Good anatomic and visual response. No serious ocular adverse drug reactions were observed/reported in the treated eye

BCVA, best-corrected visual acuity; QXW, every X weeks; VEGF, vascular endothelial growth factor.

# Case 2

| Patient History | |
|---|---|
| **Age** | 69 |
| **Sex** | Male |
| **Disease** | DME |
| **Disease Duration** | ~2 months |
| **Affected Eye(s)** | Right |
| **Ocular History** | Cataract surgery on right eye May 2023 |
| **Patient Background** | Parkinson's disease, type 2 diabetes (20 years), hypertension |

**Right Eye**

**Baseline BCVA:**
20/40

**Left Eye**

**Baseline BCVA:**
20/20

**Diagnosed With DME:**
May 2023

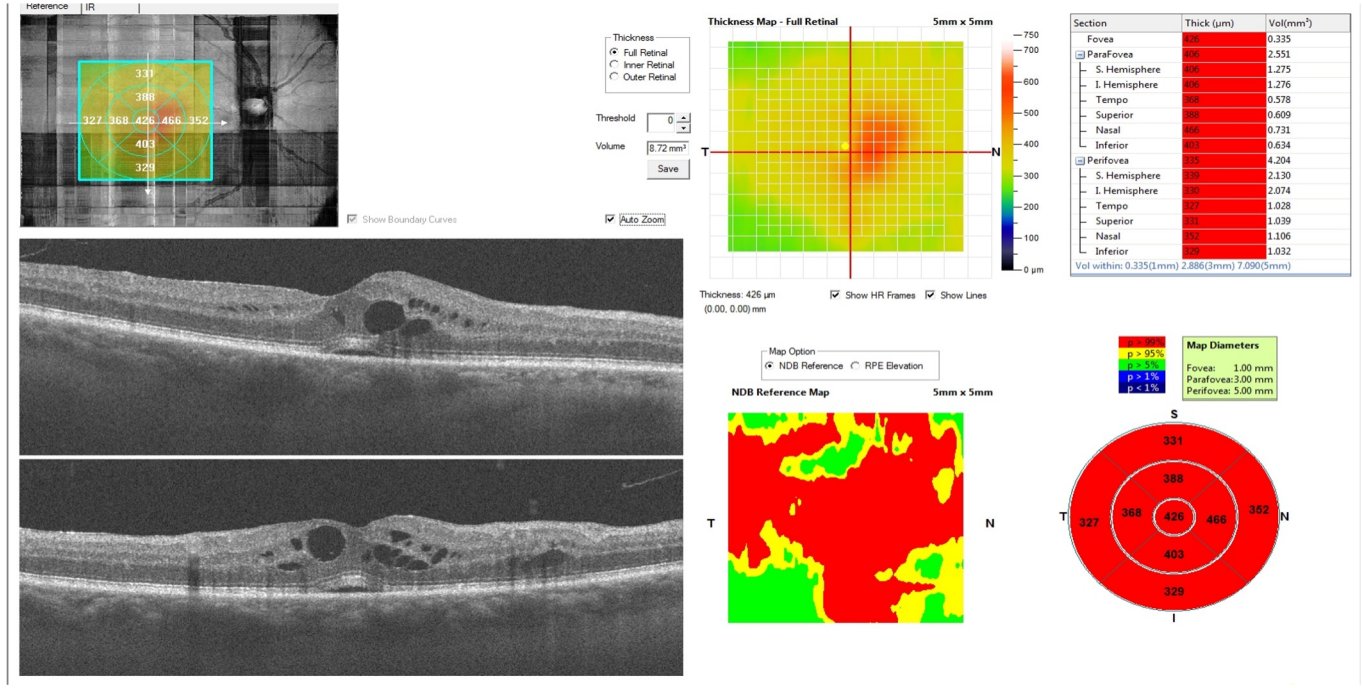
BCVA, best-corrected visual acuity; DME, diabetic macular edema.

# Case Study: Baseline

**Right Eye**

**Baseline**

**BCVA:** 20/40




**Faricimab**

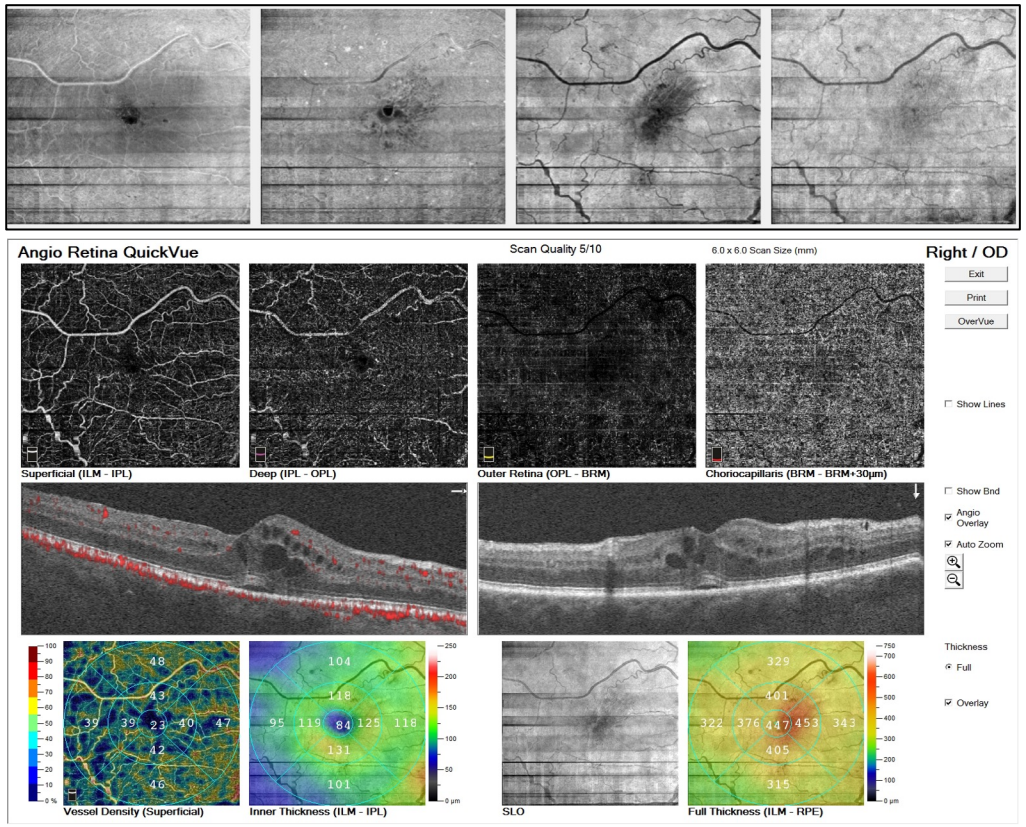
#1

Faricimab #1 given

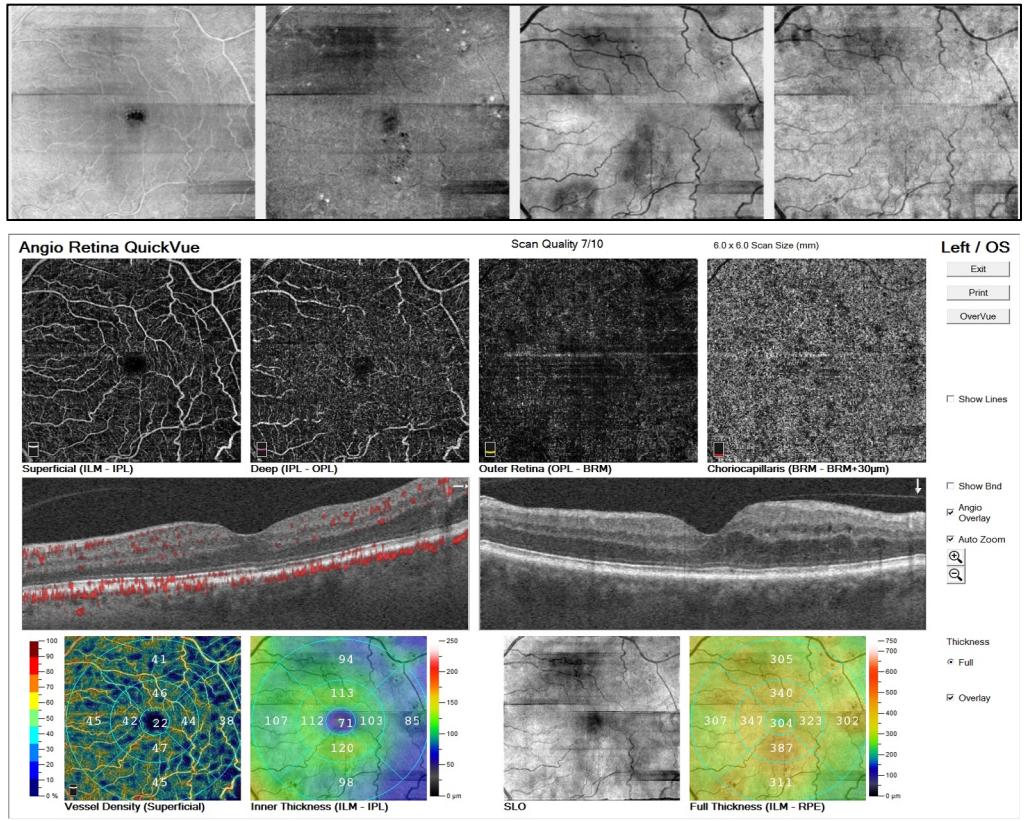
BCVA, best-corrected visual acuity.

# Case Study: Baseline

**Right Eye**




**Left Eye**




**Faricimab**

#1

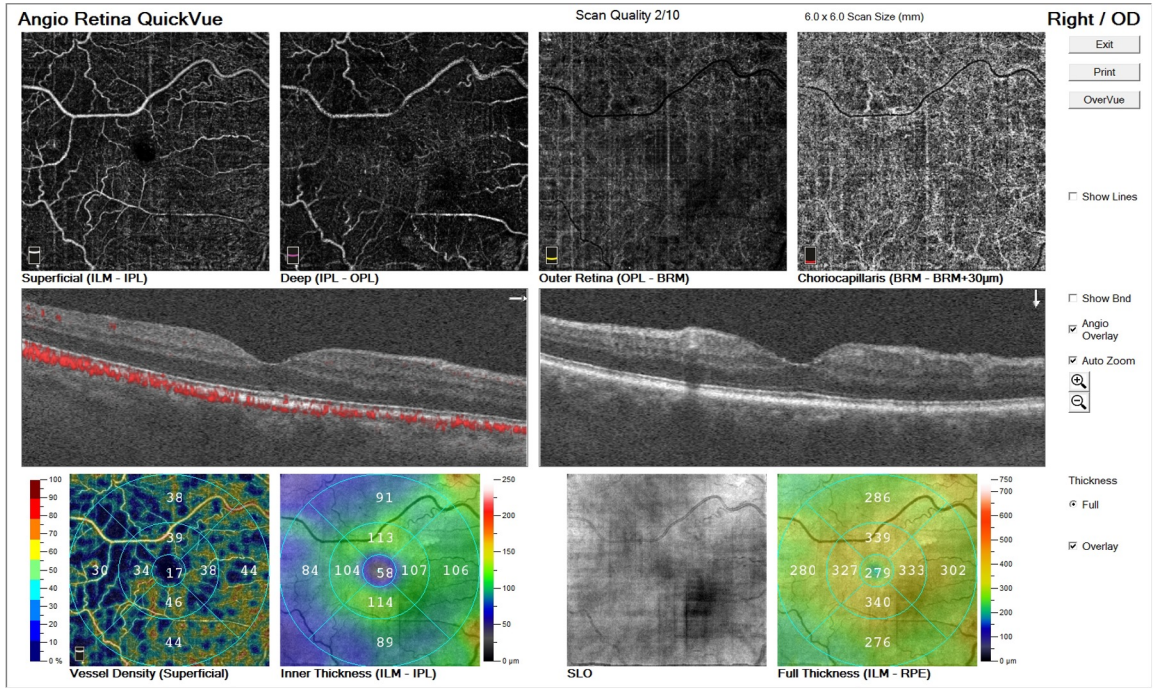
Faricimab #1 given (right eye)

# Case Study: DME In Right Eye Treated With Faricimab Q4W

**Right Eye**

**4 Weeks After Faricimab #1**

**BCVA:** 20/25




**Faricimab**

#1 **Q4W** #2

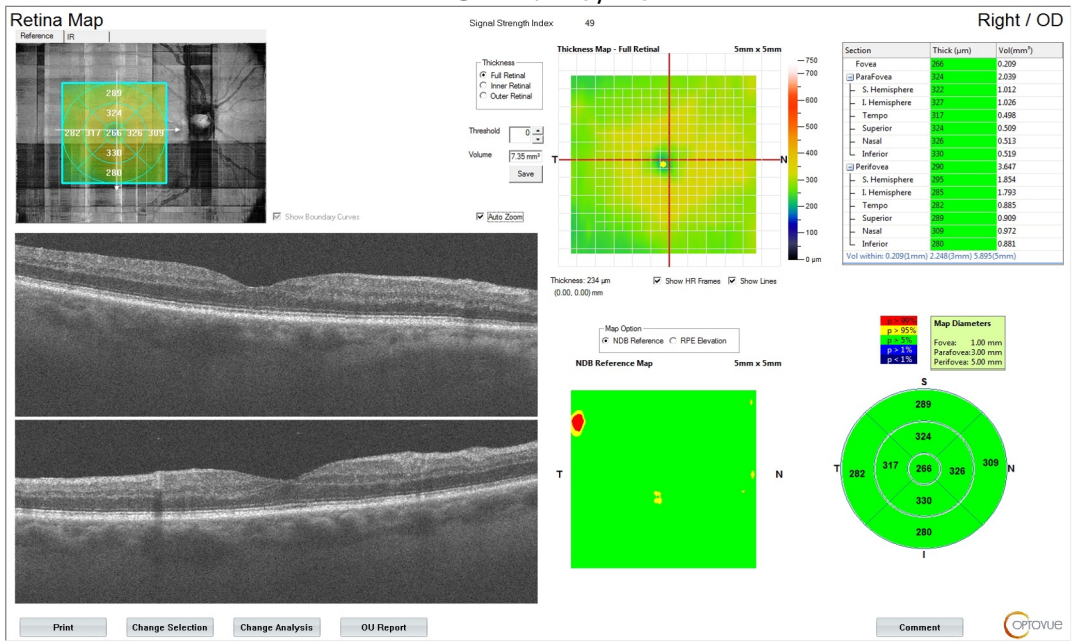
Faricimab #2 given

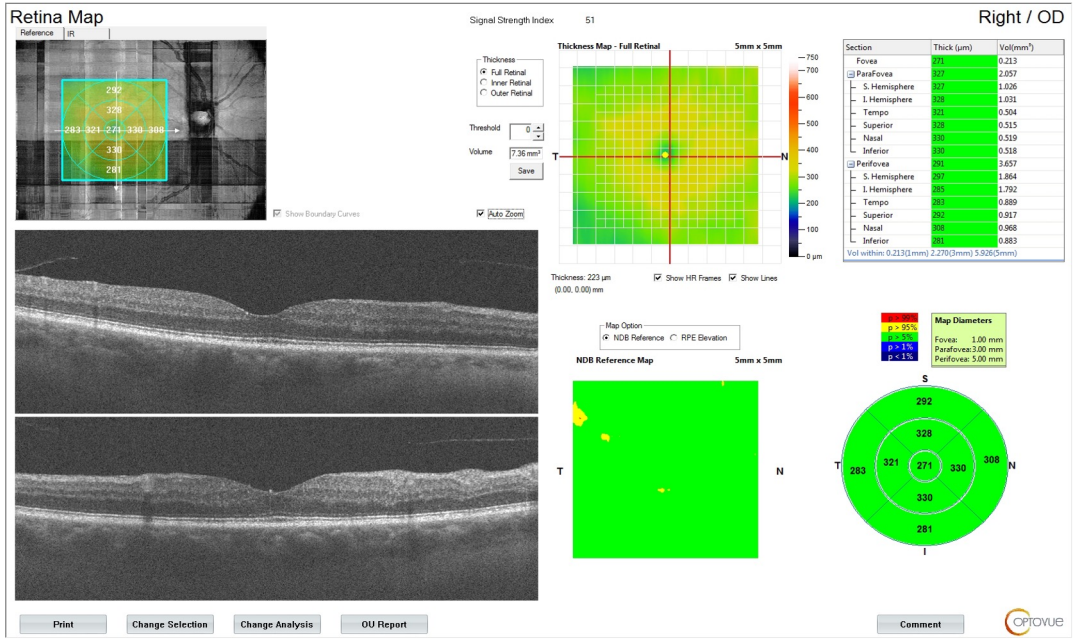
BCVA, best-corrected visual acuity; DME, diabetic macular edema; QXW, every X weeks.

# Case Study: Extended From Faricimab Q4W To Q8W, To Q12W, To Q16W

**Right Eye**

| 8 Weeks After Faricimab #4 | 12 Weeks After Faricimab #5 |
|---|---|
| **BCVA:** 20/20 | **BCVA:** 20/20 |




**Faricimab**

#1 —Q4W— #2 —Q4W— #3 —Q4W— #4 —Q8W— #5 —Q12W— #6

Faricimab #5 given

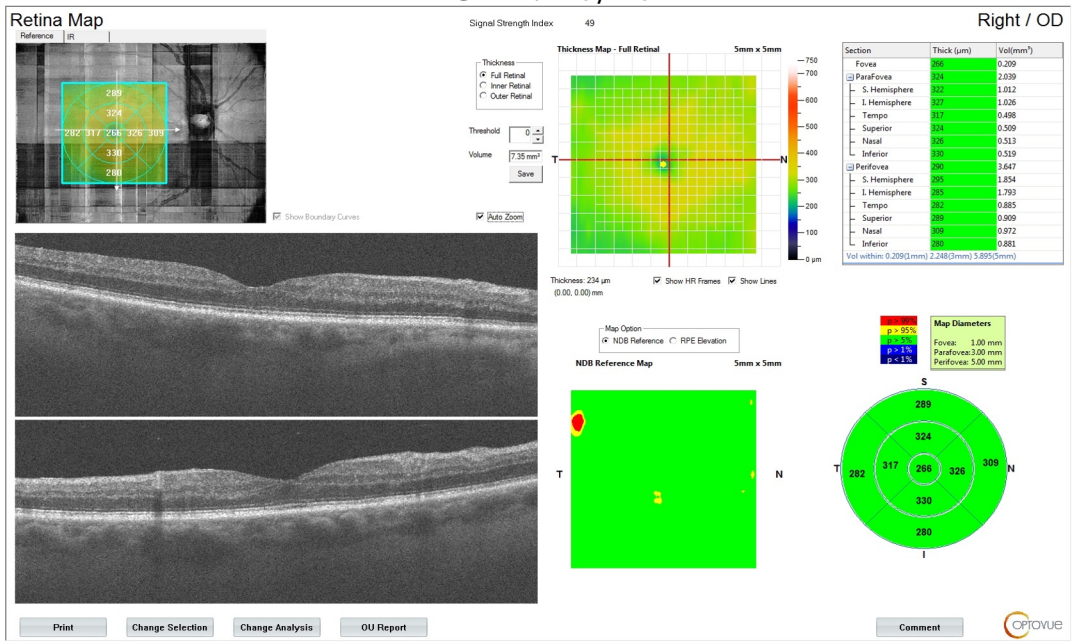
Faricimab #6 given

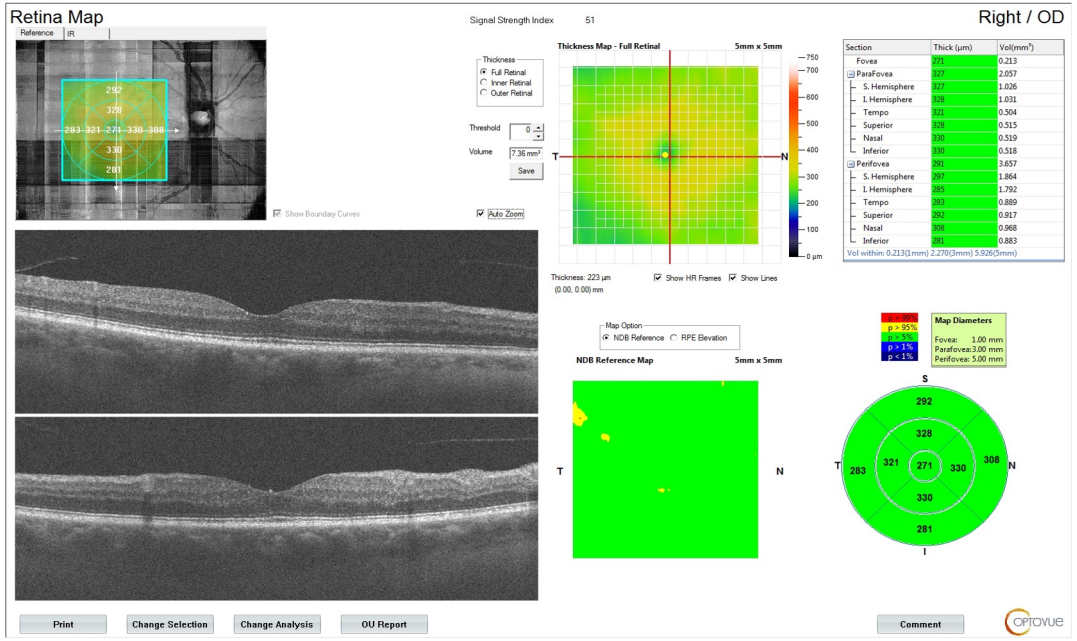
BCVA, best-corrected visual acuity; DME, diabetic macular edema; QXW, every X weeks.

# Case Study: Extended From Faricimab Q4W To Q8W, To Q12W, To Q16W

**Right Eye**

| 8 Weeks After Faricimab #4 | 12 Weeks After Faricimab #5 |
|---|---|
| **BCVA:** 20/20 | **BCVA:** 20/20 |




**Faricimab**

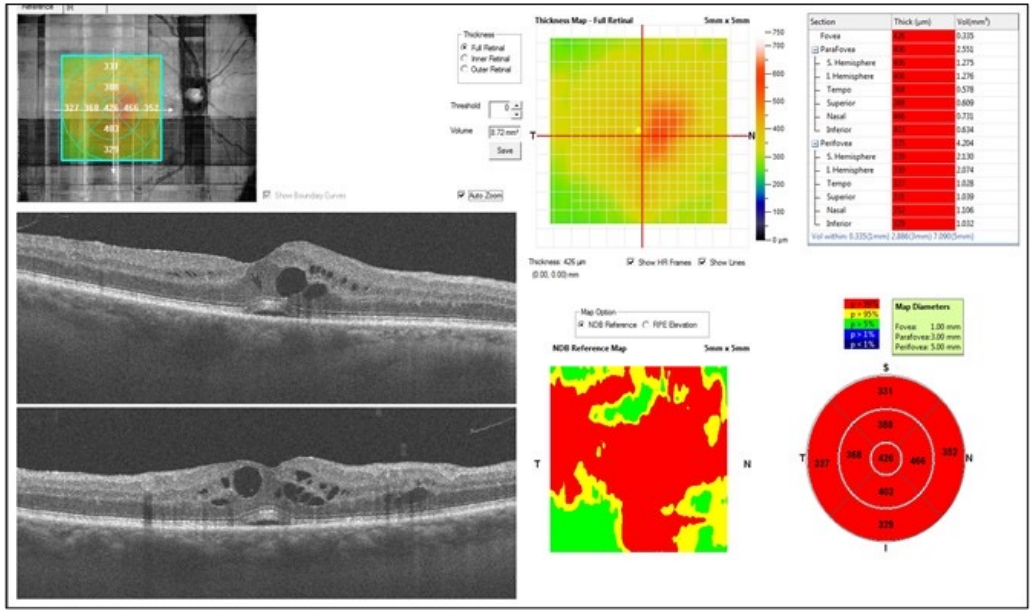
#1 —Q4W— #2 —Q4W— #3 —Q4W— #4 —Q8W— #5 —Q12W— #6 —Q16W— #7

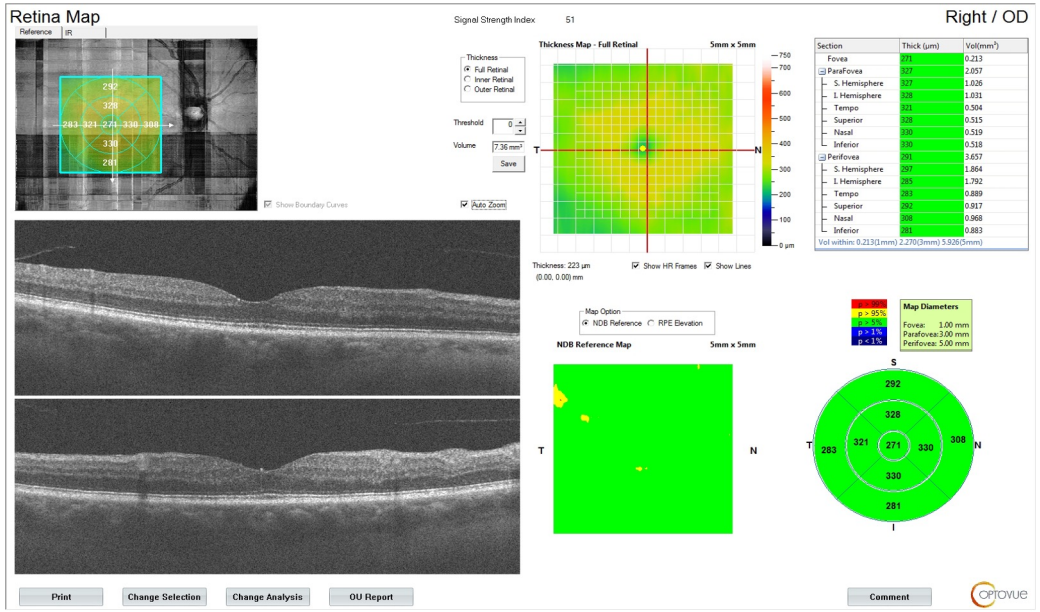
Patient has been extended to Q16W dosing

BCVA, best-corrected visual acuity; DME, diabetic macular edema; QXW, every X weeks.

# Case Study: Summary And Discussion

| Baseline | 12 Weeks After Faricimab #5 |
|---|---|
| **BCVA:** 20/40 | **BCVA:** 20/20 |



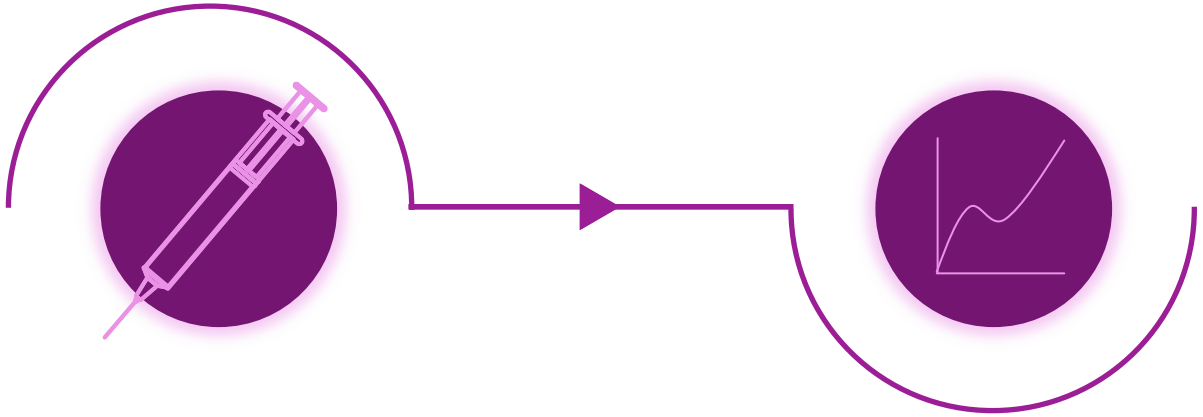



DME diagnosed after cataract surgery; peripheral hypoperfusion/ischemia in both eyes

Good response to faricimab – fast extension and well tolerated without side effects

BCVA, best-corrected visual acuity; DME, diabetic macular edema.

# Take Home Messages



Faricimab is a **bispecific antibody targeting two pathways** via inhibition of Ang-2 and VEGF-A

Clinical biomarkers show the potential **benefit of dual inhibition**, over VEGF pathway inhibition alone

Ang-2, angiopoietin-2; VECF-A, vascular endothelial growth factor A.

# Time for Some Questions!

# What is the traditional Swedish coffee break, often enjoyed with pastries, known as?

Roche

A Fika

B Smörgåsbord

C Midsommar

D Lagom


VEERAL SHETH PATRICIA UDAONDO RAJ MUKHERJEE

# What is the traditional Swedish coffee break, often enjoyed with pastries, known as?

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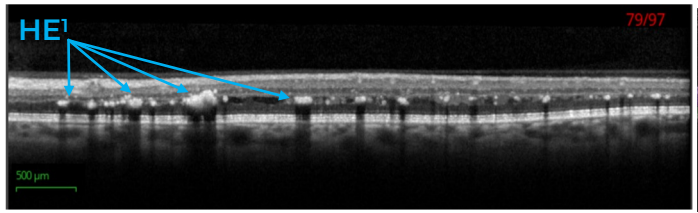
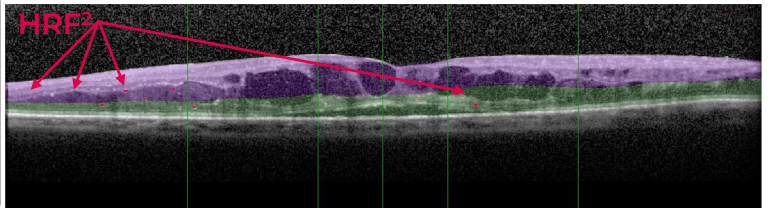
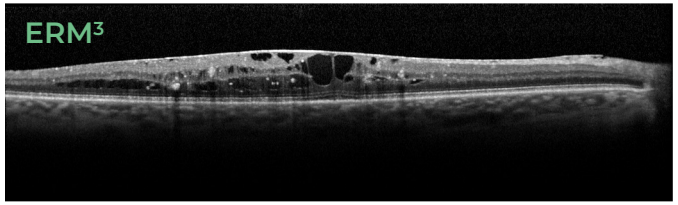
VEERAL SHETH PATRICIA UDAONDO RAJ MUKHERJEE

# In the YOSEMITE/RHINE trials, which of the following biomarkers were improved with faricimab vs aflibercept?




**A** Reduction of hard exudates

**B** Reduction HRF

**C** Reduction ERM formation

**D** All of the above

50:50

1. Goldberg RA *et al.* ARVO 2024; 2. Graff J *et al.* Hawaiian Eye and Retina Meeting 2024; 3. Jaffe GJ *et al.* ASRS 2023.

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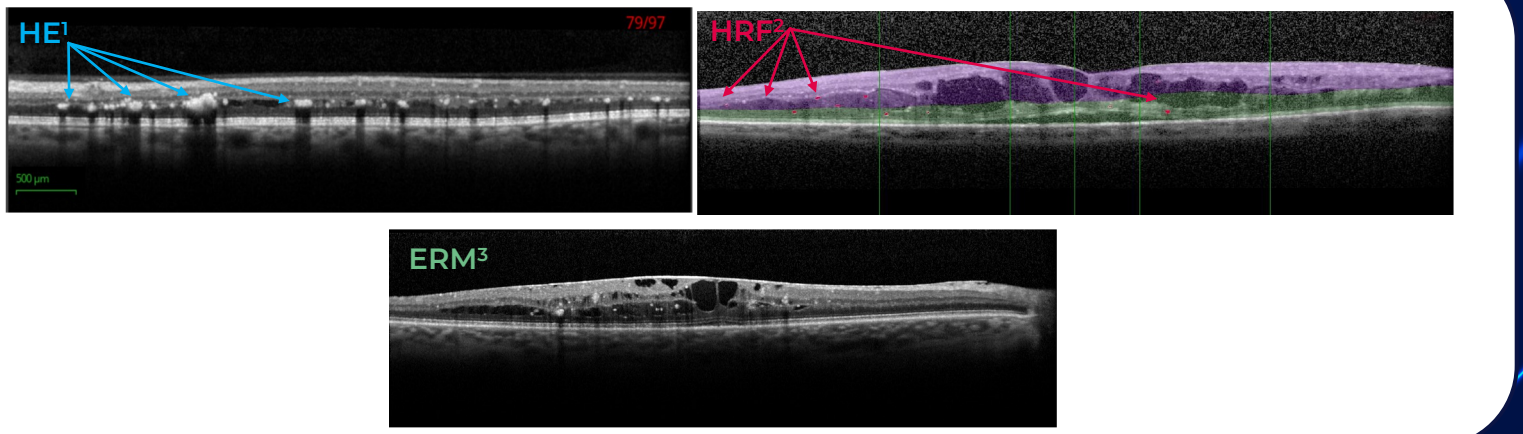


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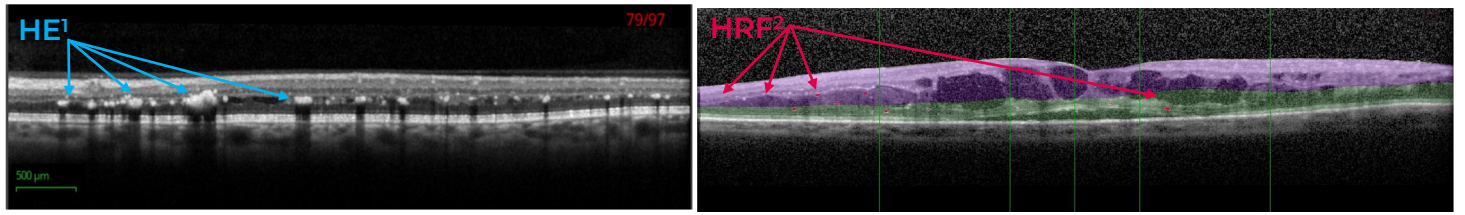





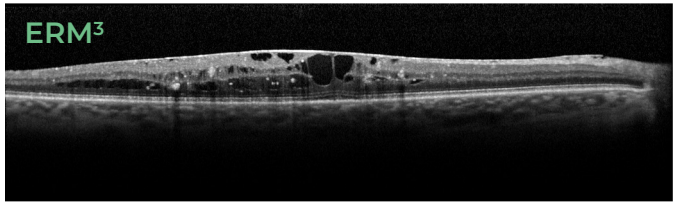


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B Reduction HRF

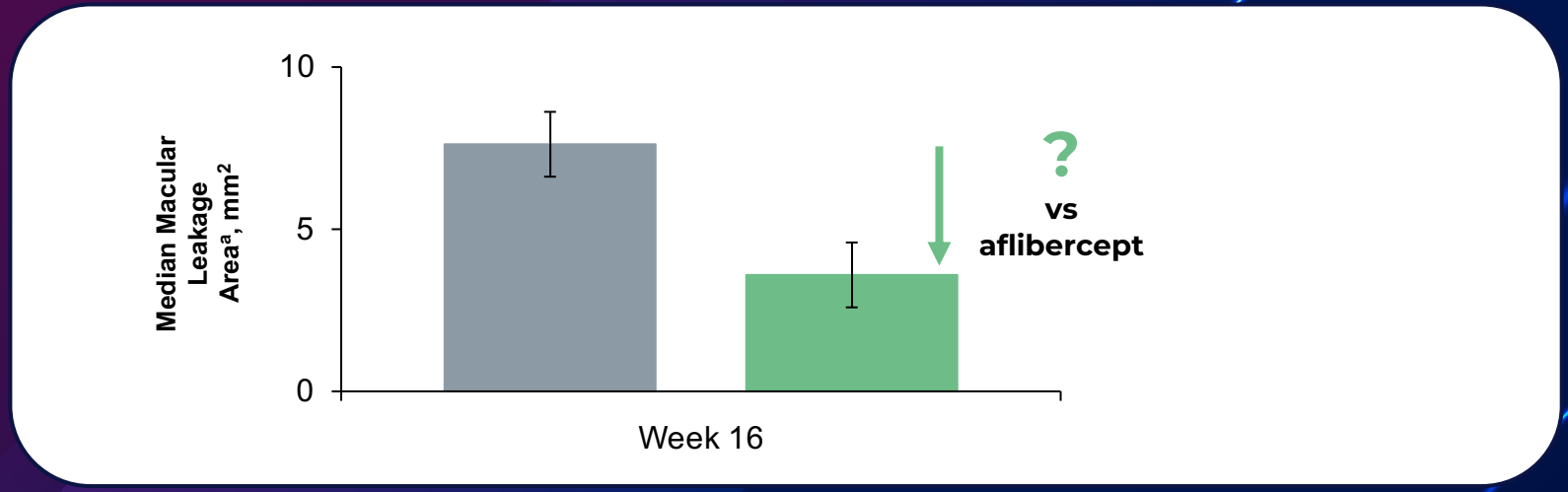
C Reduction ERM formation

D All of the above

50:50

1. Goldberg RA *et al.* ARVO 2024; 2. Graff J *et al.* Hawaiian Eye and Retina Meeting 2024; 3. Jaffe GJ *et al.* ASRS 2023.

# By what percentage did faricimab reduce macular leakage vs aflibercept at the end of the head-to-head matched dosing phase (Week 16)?




**A** 53%

**B** 47%

**C** 36%

**D** 64%

50:50

Sivaprasad S *et al.* EURETINA 2023.

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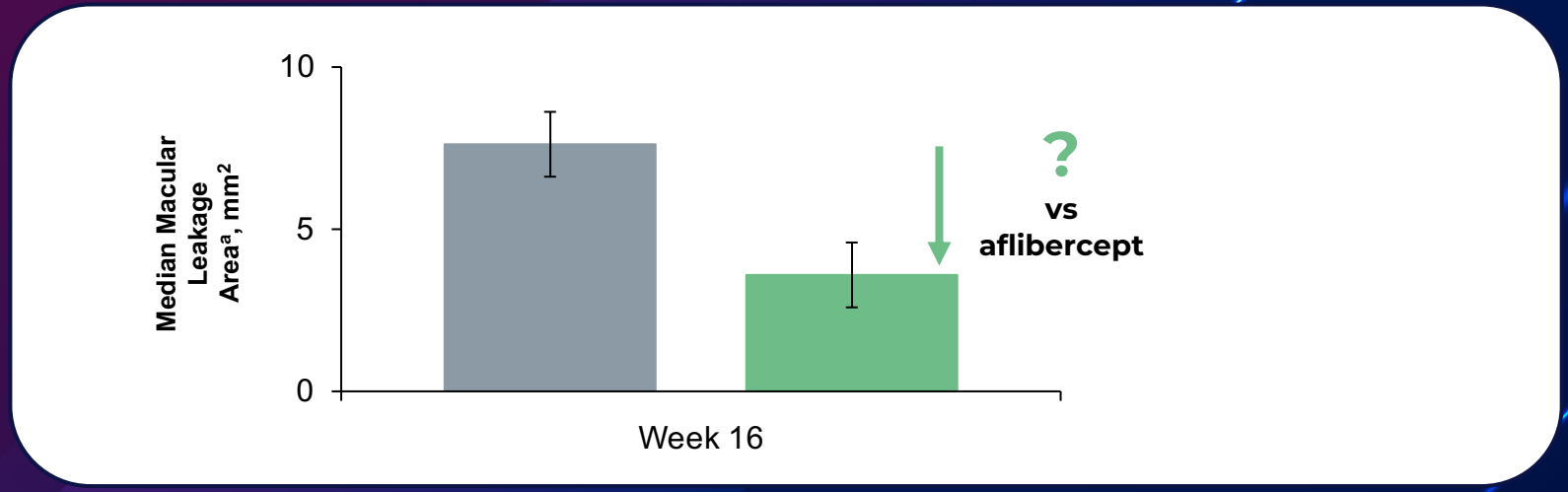


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**C** 36%

**D** 64%

50:50

Sivaprasad S *et al.* EURETINA 2023.

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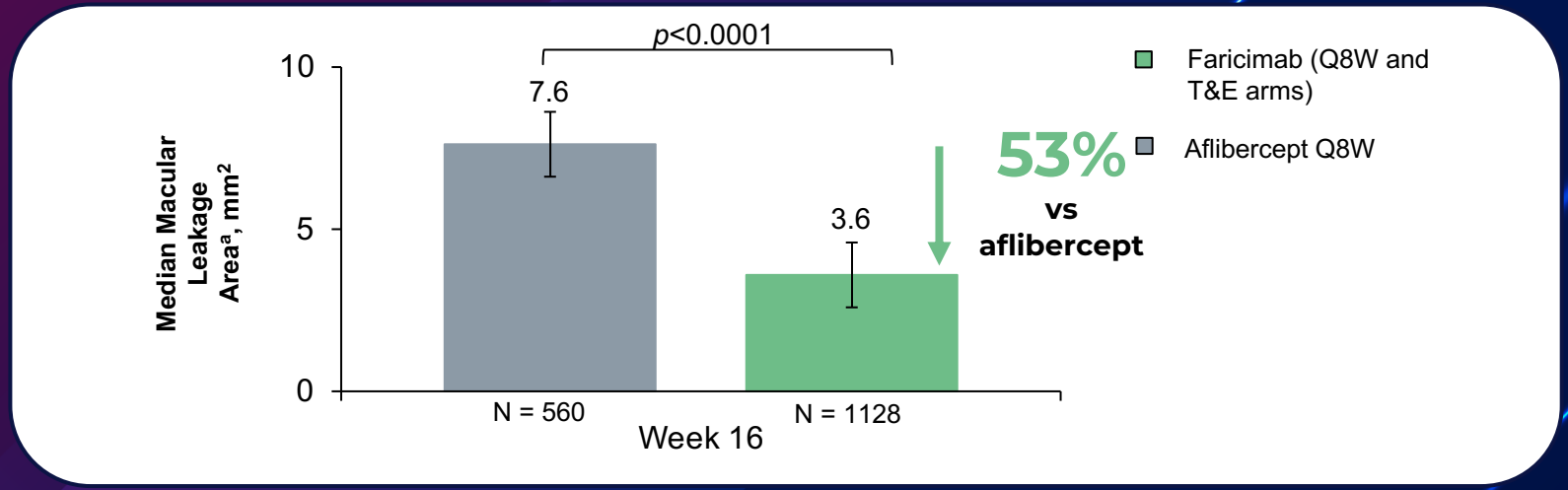



A 53%

B 47%

C 36%

D 64%

50:50

Sivaprasad S *et al.* EURETINA 2023.

# Round 1

1 / 3

PATRICIA UDAONDO

1 / 3

RAJ MUKHERJEE

1 / 3

VEERAL SHETH

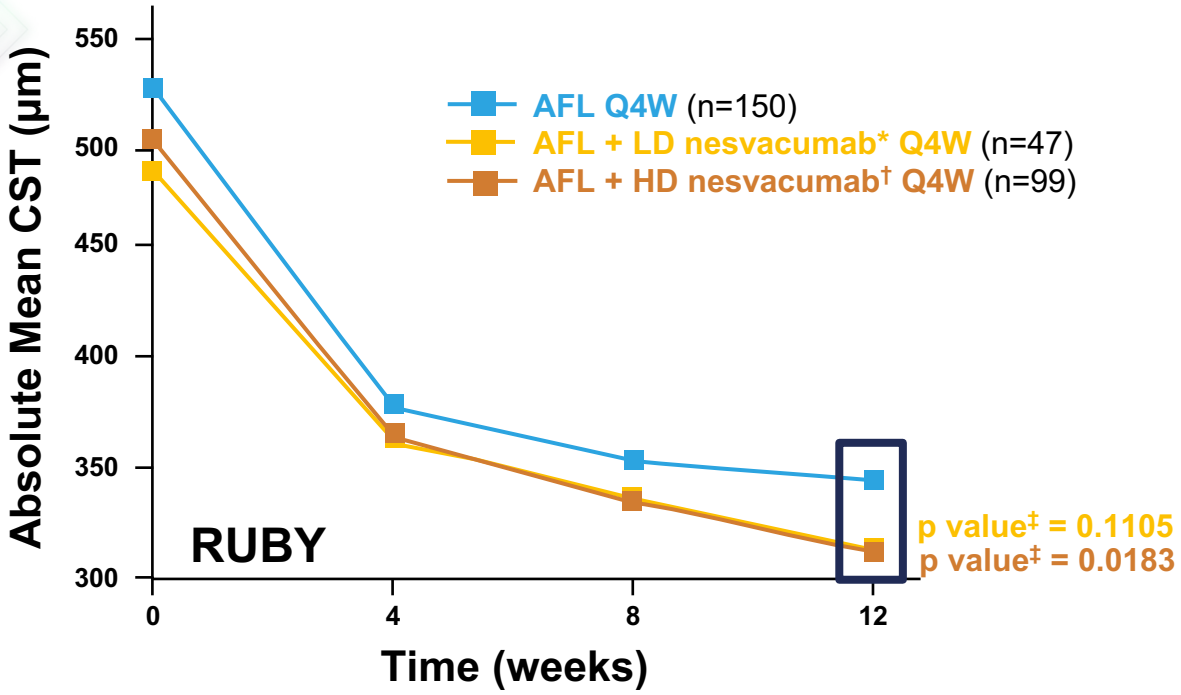
# Drying: Achieving Disease Control


## Veeral Sheth

Partner and Director of Clinical Research
University Retina and Macula Associates, Chicago, Illinois, USA

# Targeting Ang-2 Together With VEGF Improves Anatomic Outcomes[1]

## Aflibercept + nesvacumab (anti–Ang-2) combination therapy



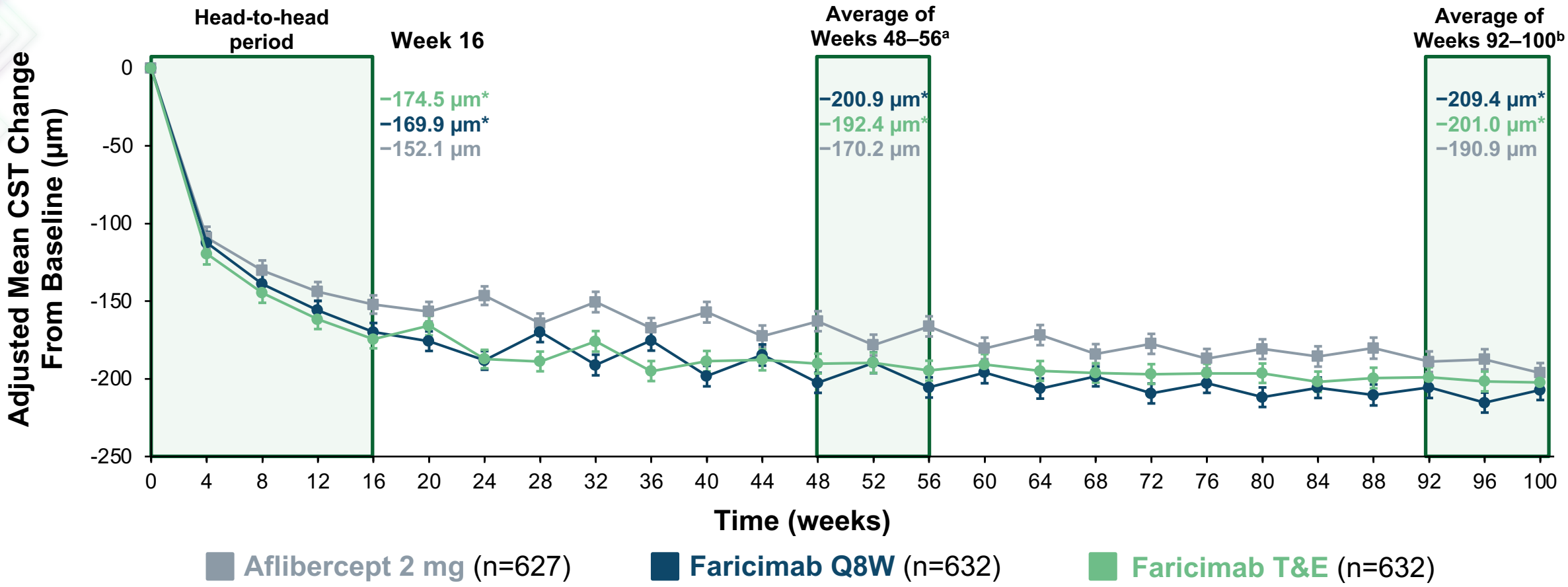

*"Indication of additional anatomic benefit with combination therapy"* [1]

*"...positive anatomic effects may warrant further investigation of the role of anti–Ang-2 agents in combination with anti-VEGF therapy"* [1]

*LD combination nesvacumab 3.0 mg + AFL 2.0 mg; †HD combination nesvacumab 6.0 mg + AFL 2.0 mg; ‡p-values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on p-values; comparison vs aflibercept Q4W. Clinical significance has not been established and conclusions regarding treatment effect cannot be drawn. Reprinted from Wolters Kluwer, 42 (6), Brown DM, et al., Intravitreal nesvacumab (angiopoietin 2) aflibercept in diabetic macular edema: Phase 2 RUBY randomized trial, 1111–20, Copyright (2022), with permission from Wolters Kluwer. AFL, aflibercept; Ang-2, angiopoietin-2; CST, central subfield thickness; HD, high-dose; LD, low-dose; QxW, every X weeks; VEGF, vascular endothelial growth factor. 1. Brown DM, *et al.* Retina. 2022;42:1111–20.

# Greater Reductions In CST With Faricimab Vs Aflibercept In The Head-to-head Period And During Year 1 And Year 2[1,2,*]

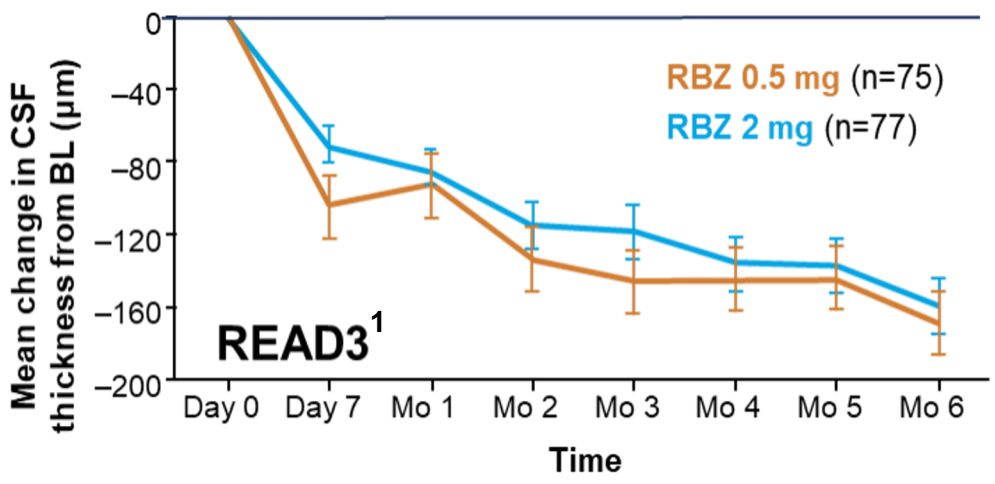
## YOSEMITE/RHINE pooled



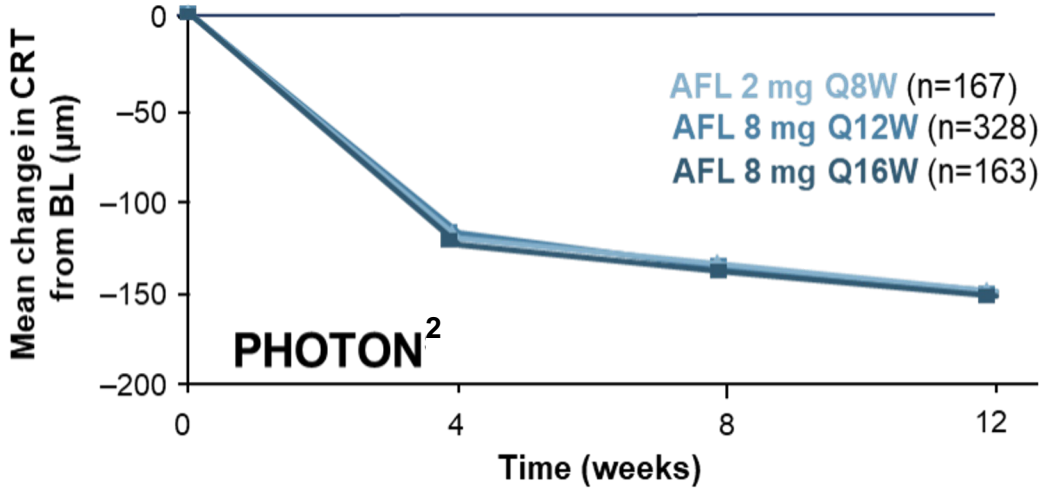

*P values are nominal and not adjusted for multiplicity (nominal p value <0.05 vs aflibercept 2 mg Q8W); no formal statistical conclusion should be made based on the P values. [a]Adjusted mean change from baseline at year 1, averaged over weeks 48, 52, and 56. [b]Adjusted mean change from baseline at year 2, averaged over weeks 92, 96, and 100. Results are based on a mixed model for repeated measures analysis, adjusted for treatment group, visit, visit-by-treatment group interaction, baseline CST (continuous), baseline BCVA (<64 vs ≥64 ETDRS letters), prior intravitreal anti-VEGF therapy (yes vs no), region (United States and Canada, Asia, and rest of the world), and study (YOSEMITE vs RHINE). 95% CI error bars are shown. BCVA, best-corrected visual acuity; CI, confidence interval; CST, central subfield thickness; DME, diabetic macular edema; T&E, treat-and-extend; QxW, every X weeks. 1. Manoharan N *et al.* ARVO 2024. 2. Wong TY *et al.* Ophthalmology. 2024;131(6):708-723.

# Increasing The Dose Of Anti-VEGF By Four Times Did Not Improve Fluid Reduction

## 4× Ranibizumab Dose




## 4× Aflibercept Dose




Reprinted from Springer Nature, 29 (12), Do DV et al., Month-6 primary outcomes of the READ-3 study, 1538-1544, Copyright (2023), with permission from Springer Nature. AFL, aflibercept; BL, baseline; CRT, central retina thickness; CSF, central subfield; Mo, month; QXW, every X weeks; RBZ, ranibizumab; VEGF, vascular endothelial growth factor. 1. Do DV *et al.* Eye. 2015;29:1538–1544; 2. Brown DM *et al.* AAO 2022.

# Increasing The Dose Of Anti-VEGF By Four Times Did Not Improve Fluid Reduction

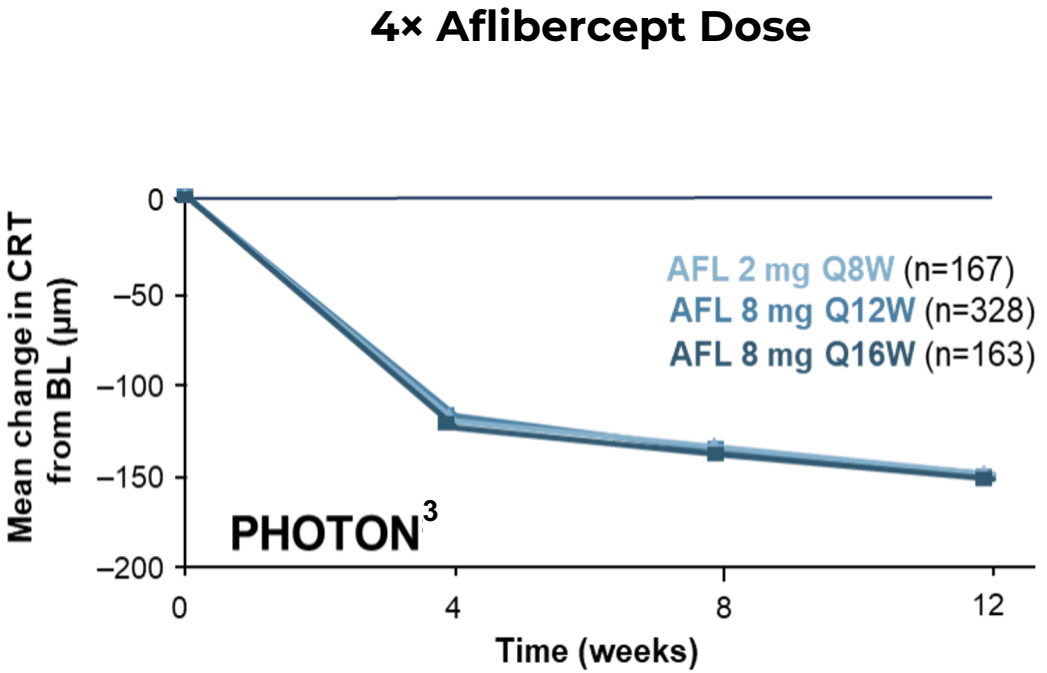
**EMA**

"As the IVT dose increased from 2 mg of aflibercept to 8 mg of HD aflibercept, **no further increase in PD effect (decrease in CRT) was observed** 4 weeks after each initial Q4W dose through 12 weeks"[1]

**FDA**

"The study **did not establish consistent treatment benefit of the high doses of aflibercept** in retinal fluid dryness compared to the active control."

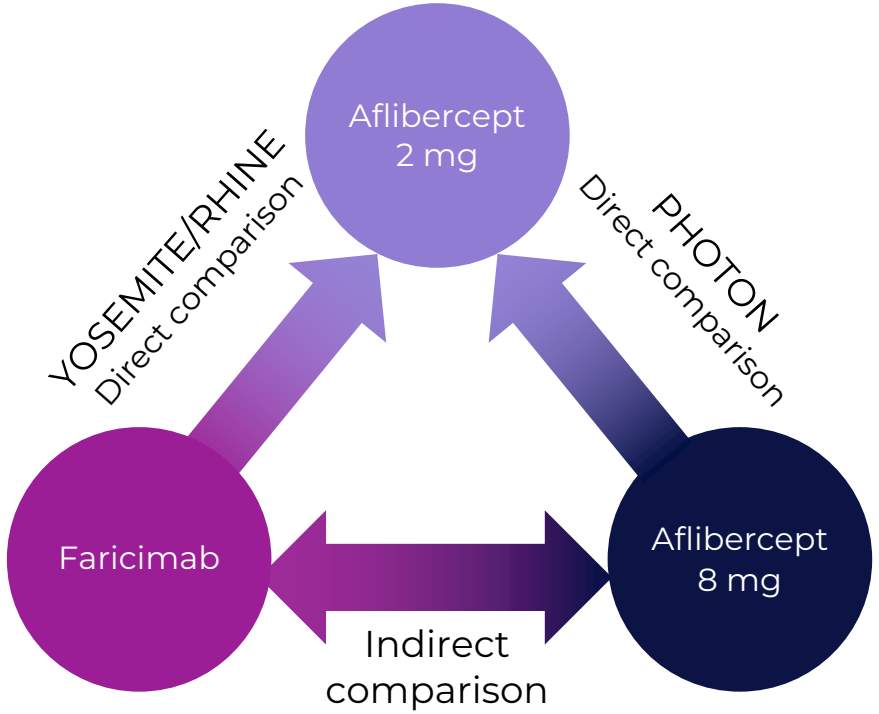
"The clinical benefit of HD of aflibercept in retinal fluid dryness compared to 2q8 is **questionable**"[2]



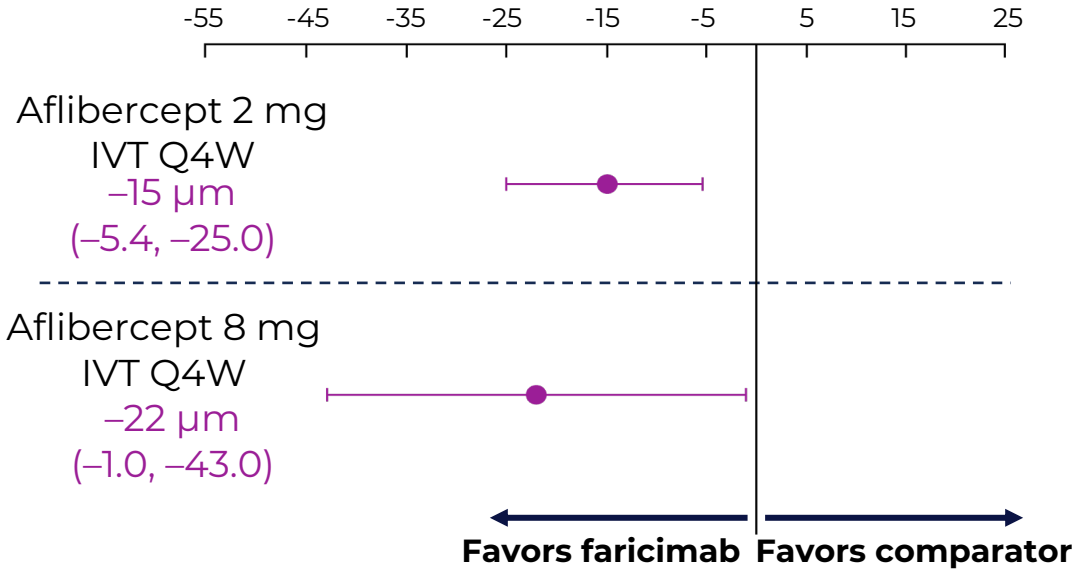

AFL, aflibercept; BL, baseline; CRT, central retina thickness; DME, diabetic macular edema; EMA, European Medicines Agency; FDA, Food and Drug Administration; HD, high dose; IVT, intravitreal; PD, pharmacodynamic; nAMD, neovascular age-related macular degeneration; QXW, every X weeks; VEGF, vascular endothelial growth factor. 1. European Medicines Agency. Eylea Assessment Report 2023; 2. Center for Drug Evaluation and Research, Application Number: 761355Orig1s000, Summary Review; 3. Brown DM *et al.* AAO 2022.

# Faricimab Was Associated With Greater CST Improvements Vs Aflibercept 2 mg Or 8 mg At 12 Weeks[1]

## Network Meta-Analyses Comparing Faricimab And Aflibercept



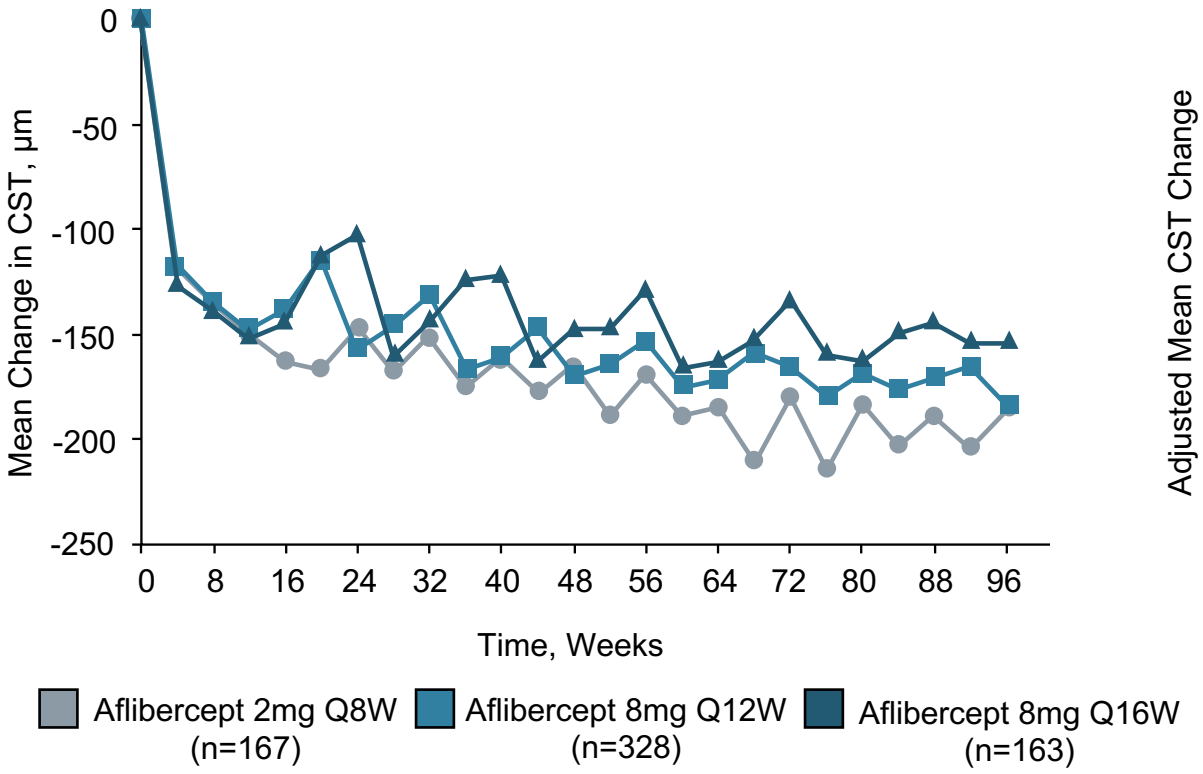

Mean difference in CST change from baseline, µm (RE model, 95% CrI) for faricimab 6.0 mg IVT Q4W vs:




As there are no direct comparative studies between faricimab and aflibercept 8 mg, an indirect comparison using NMA provides a scientifically sound method to identify differences. However, NMAs do not replace clinical studies. The analysis of the included studies with regard to possible effect modifiers (e.g. study or patient characteristics such as BCVA or central subfield/retinal thickness) showed that there were no substantial differences (similarity assumption). Prior information in the form of a priori distributions was used. PHOTON measured CRT. BCVA, best corrected visual acuity; CrI, credible interval; CRT, central retina thickness; CST, central subfield thickness; IVT, intravitreal; NMA, network meta-analysis; QXW, every X weeks; RE, random effects. 1. Leng T. Macula Society Annual Meeting 2024.

# 8 mg Aflibercept Patients Treated At Q16W Had More Fluid And Fluctuations Than 2 mg Aflibercept

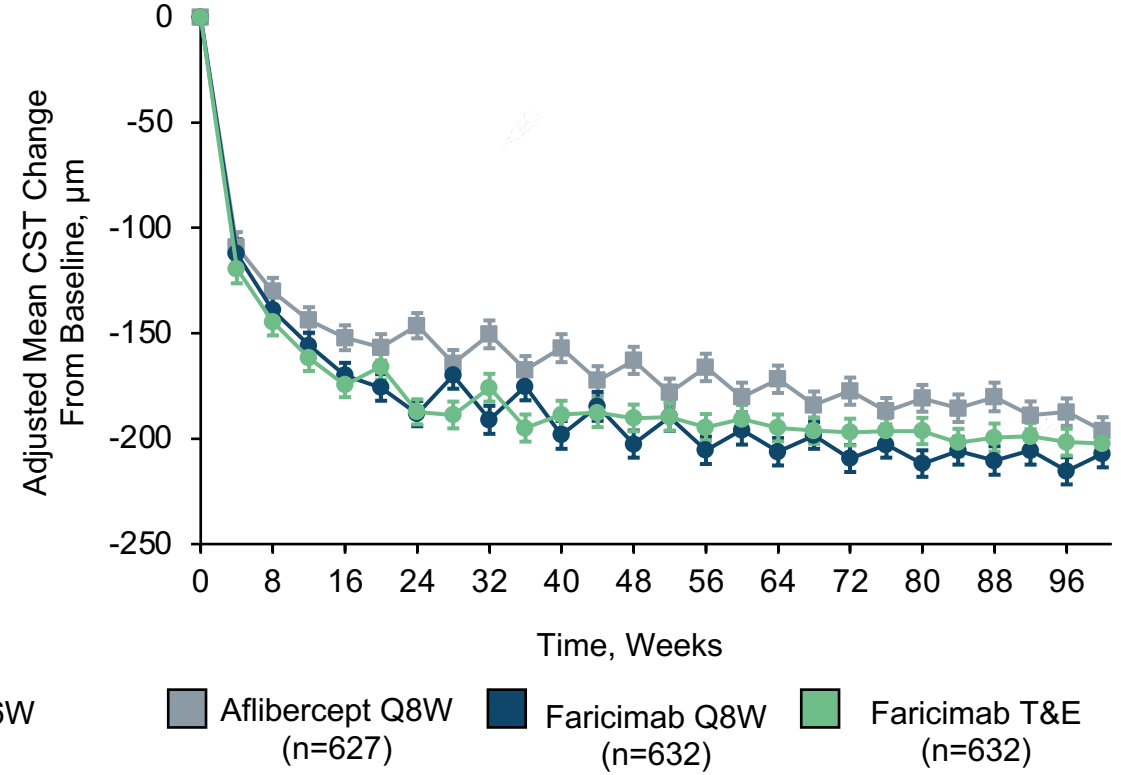
## PHOTON[1]




**Lancet Commentary**

"[Potential] undertreatment of diabetic retinopathy in the aflibercept 8q16 group."[4]

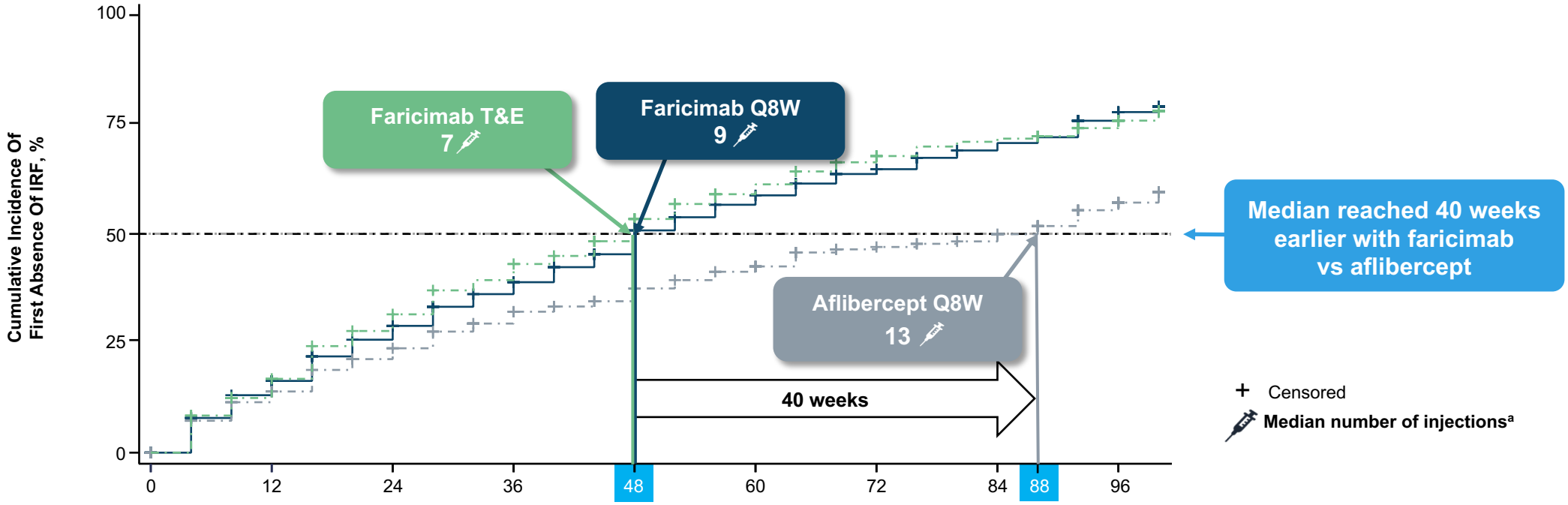
## YOSEMITE & RHINE[2,3]




This is not a cross-trial comparison. CST, central subfield thickness; QXW, every X weeks; T&E, treat-and-extend. 1. Do DV. ASRS 2023; 2. Wykoff C *et al.* Lancet. 2022;399:741–755; 3. Baumal C *et al.* ARVO 2022; 4. Gabrielle PH & Creuzot-Garcher. Lancet. 2024;403(10432):1111-1113.

# Nine Months Faster Median Time To First Absence Of IRF With Faricimab vs Aflibercept[1]

## YOSEMITE/RHINE pooled post hoc analysis




| Patients at risk | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Aflibercept Q8W | 611 | 534 | 470 | 411 | 375 | 331 | 291 | 277 | 227 | |
| Faricimab Q8W | 621 | 532 | 445 | 373 | 310 | 241 | 196 | 163 | 122 | HR (95% CI)[b]: 1.62 (1.40, 1.88), *p*<0.0001 |
| Faricimab T&E | 618 | 533 | 431 | 357 | 300 | 233 | 187 | 160 | 136 | HR (95% CI)[b]: 1.65 (1.42, 1.91), *p*<0.0001 |

Patients with IRF at baseline. Summaries of time to first absence of IRF are Kaplan-Meier estimates. Patients with absence of IRF at baseline and patients with no data at baseline were excluded from the analysis. P values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the P values. Statistics for pairwise comparisons were calculated using a separate model for each comparison. HRs were estimated by Cox regression. Statistical analyses were stratified by baseline BCVA (< 64 vs ≥ 64 letters), prior intravitreal anti-VEGF therapy (yes vs no), region (United States and Canada, Asia, and the rest of the world) and study (YOSEMITE vs RHINE). [a]The number of injections includes any active drug administered (faricimab or aflibercept), including medication errors. [b]Results from stratified analyses are presented for HR and log-rank test vs aflibercept. An HR >1 favors faricimab over aflibercept. BCVA, best-corrected visual acuity; CI, confidence interval; HR, hazard ratio; IRF, intraretinal fluid; Q8W, every 8 weeks; T&E, treat-and-extend; VEGF, vascular endothelial growth factor.

1. Manoharan N *et al.* ARVO 2024.

# Retinal Drying Is Important For Improved Visual Outcomes

## Recent evidence of fluid linked to vision outcomes in DME

### Khoramnia et al. 2024[1]
*Review*

Significant correlation between **increased fluctuations in CSFT** over the course of anti-VEGF treatment and **worse visual outcomes**

### Kalur et al. 2023[2]
*Retrospective cohort study*

The **highest quartile of total retinal fluid, IRF, and SRF volumes led to worse visual outcomes** after 12 months of anti-VEGF treatment

### Protocol I 2020[3]
*Post hoc analysis*

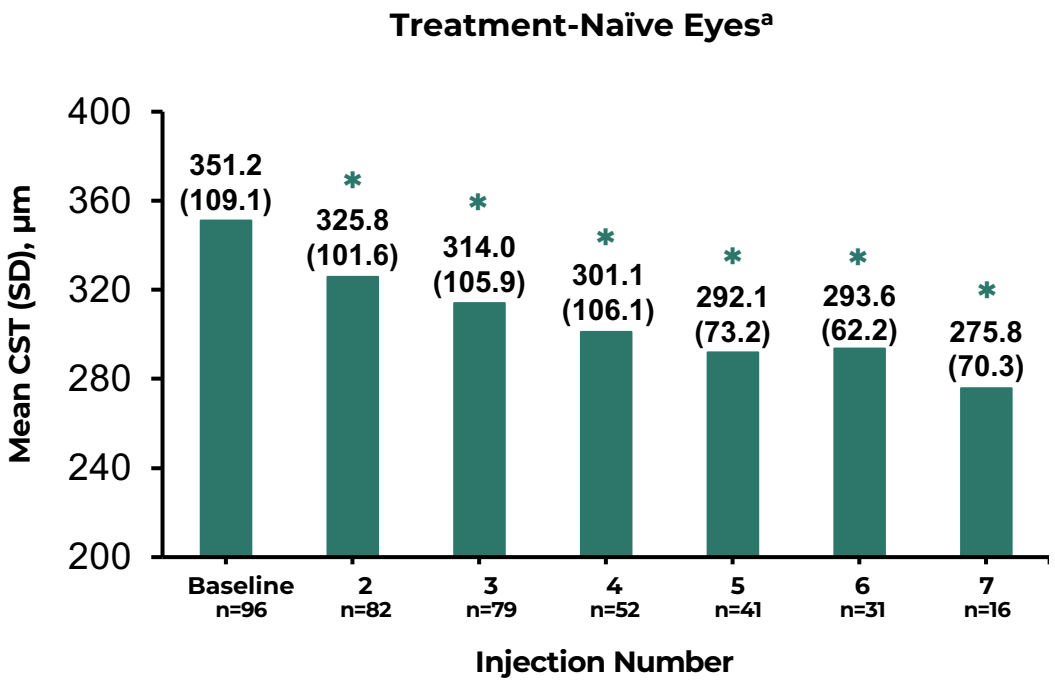
Macular edema exposure over the first 52 weeks of ranibizumab treatment was **predictive of reduced long-term visual acuity improvement**

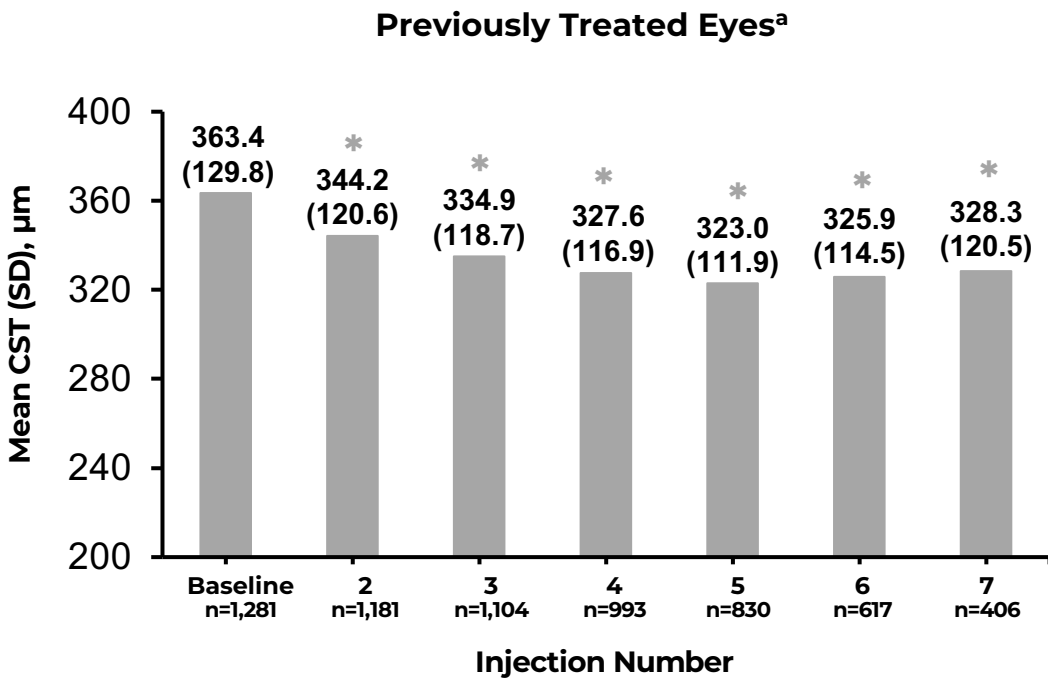
### YOSEMITE and RHINE 2024[4]
*Post hoc analysis*

**Greater IRF volume reduction** after 1 injection was associated with **improved anatomical and visual outcomes** at 1 year

CSFT, central subfield thickness; DME, diabetic macular edema; IRF, intraretinal fluid; SRF, subretinal fluid; VEGF, vascular endothelial growth factor. 1. Khoramnia R *et al.* Eye. 2024;38:54–60; 2. Kalur A *et al.* Canadian J Ophtha. 2023;58:271–277; 3. Sadda SR *et al.* Eye. 2020;34:480–490; 4. Wang Y *et al.* ARVO 2024.

# FARETINA IRIS Registry (US): Mean CST Improved In Previously Treated And Treatment-Naïve Eyes In Patients With DME[1]




*P-values calculated for change in CST from baseline. Nominal *p* value < 0.05 vs baseline. *p* values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the *p* values. [a]Among eyes with a baseline CST measurement (0–30 days before index) (n = 1377) between February 7, 2022 and June 30, 2023, and 2+ CST measures in ≤ 180 days before index and 2+ CST in 180 days post index, excluding CST measurements ≤ 14 days after an injection. Approximately 16% of faricimab patient-eyes had CST measurements available in the IRIS® Registry. CST, central subfield thickness; DME, diabetic macular edema; SD, standard deviation.

1. Borkar D *et al.* ARVO 2024.

# Summary Of Experience With Faricimab

**Started treating** DME patients with faricimab since its approval in **February 2022**

Our **first patients were switch patients**, mostly switched from aflibercept and bevacizumab

Currently, we have a total of **255 DME patients** being treated with faricimab

**157 switch patients**

**98 treatment-naïve patients**

DME, diabetic macular edema.

# Case Study: Overview

| Patient History | |
|---|---|
| **Age** | 45 years |
| **Sex** | Female |
| **Disease** | DME |
| **Disease Duration** | 2 years (diagnosed 20 Oct 2021) |
| **Affected Eye(s)** | Left eye |
| **Ocular History** | No ocular history |
| **Patient Background** | 10-year history of type 2 diabetes |

**Left Eye**

**Diagnosed With DME:**
20 October 2021

**Baseline BCVA:**
20/50

**No treatment history**

Offered anti-VEGF after diagnosis but declined

Lost to follow-up for 10 months post-diagnosis

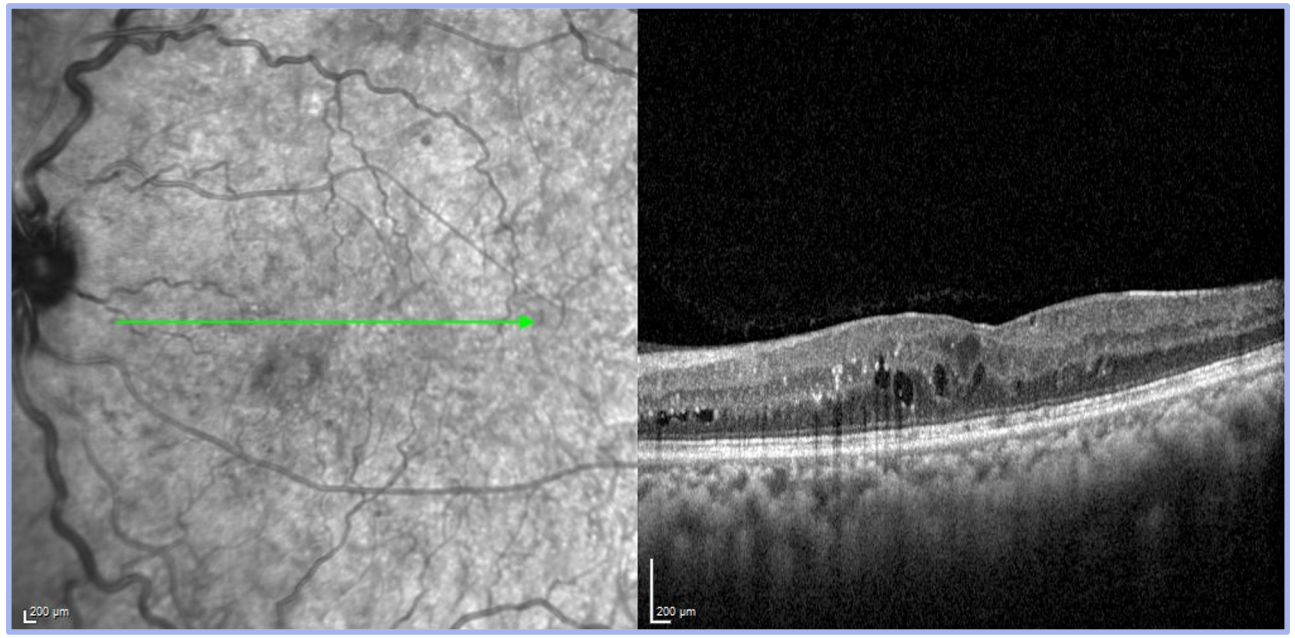
BCVA, best-corrected visual acuity; DME, diabetic macular edema; VEGF, vascular endothelial growth factor.

# Case Study: Diagnosed With DME

**Left Eye**

**Patient First Seen And Diagnosed With DME**
20 October 2021

**BCVA:** 20/50 **CST:** 397 µm




Declined anti-VEGF therapy and lost to follow-up for 10 months

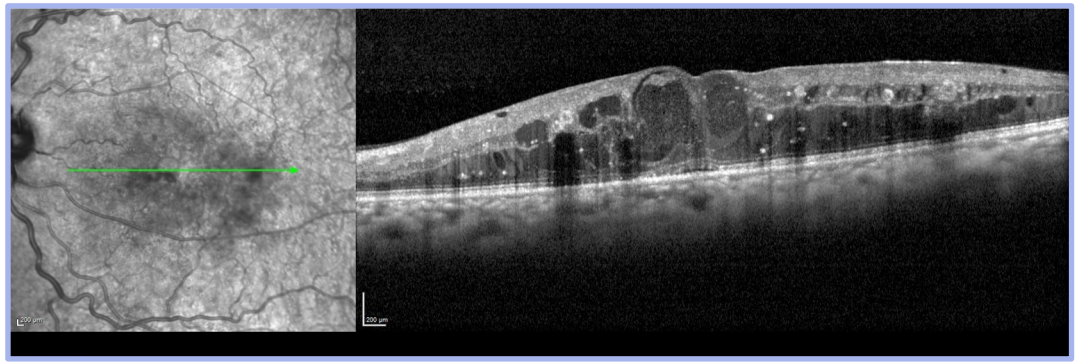
BCVA, best-corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; VEGF, vascular endothelial growth factor.

# Case Study: DME In Left Eye Treated With Faricimab Q4W

**Left Eye**

**Return To Clinic After 10 Months**
03 August 2022

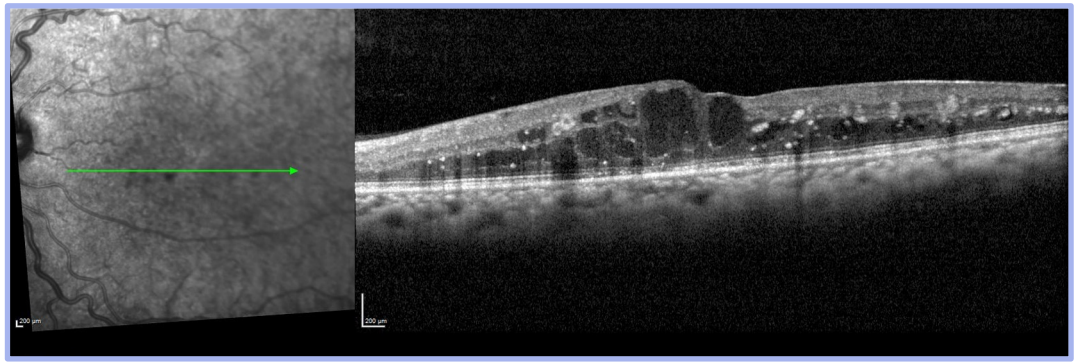
**BCVA:** 20/80 **CST:** 625 µm



Faricimab #1 given

**4 Weeks After Faricimab #1**
31 August 2022

**BCVA:** 20/60 **CST:** 478 µm



Faricimab #2 given

**Faricimab** #1 Q4W #2

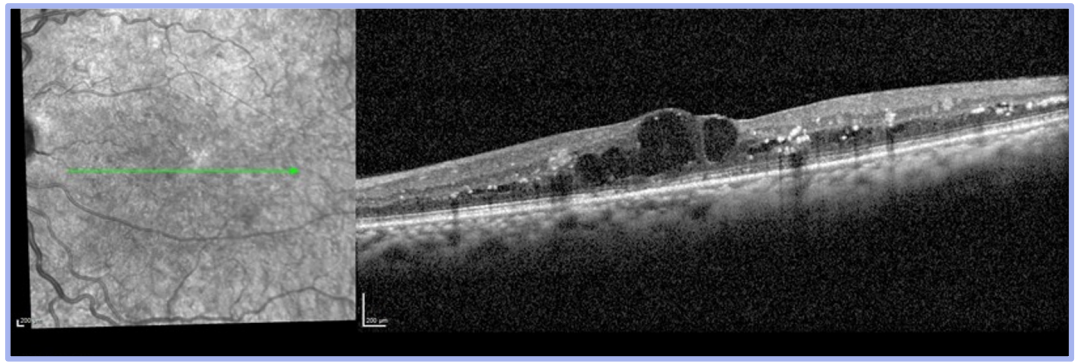
BCVA, best-corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; QXW, every X weeks.

# Case Study: Extended From Faricimab Q4W To Q8W

**Left Eye**

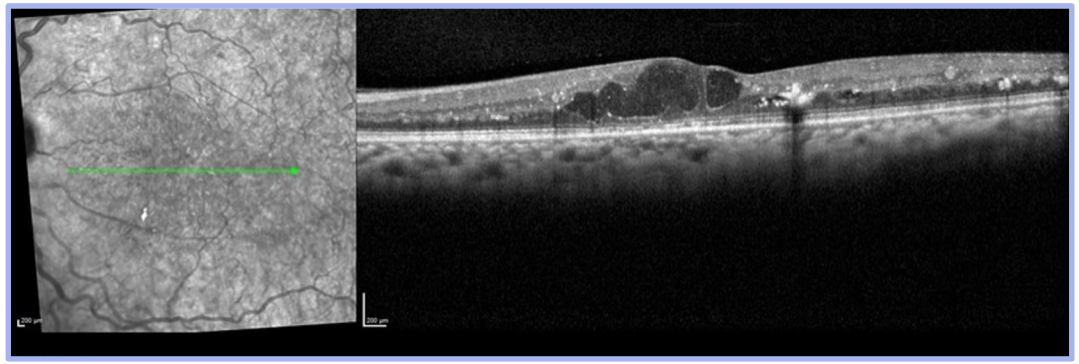
**4 Weeks After Faricimab #2**
28 September 2022

**BCVA:** 20/50 **CST:** 400 µm



**4 Weeks After Faricimab #3**
26 October 2022

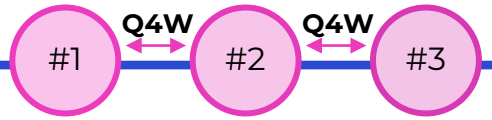
**BCVA:** 20/40 **CST:** 369 µm



Faricimab #3 given

Faricimab #4 given, and patient extended to Q8W for faricimab #5

**Faricimab**



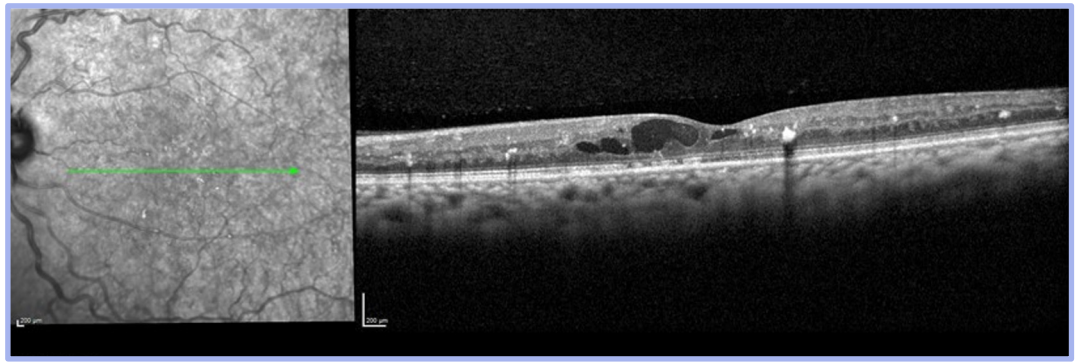

BCVA, best-corrected visual acuity; CST, central subfield thickness; QXW, every X weeks.

# Case Study: Extended From Faricimab Q8W To Q16W

**Left Eye**

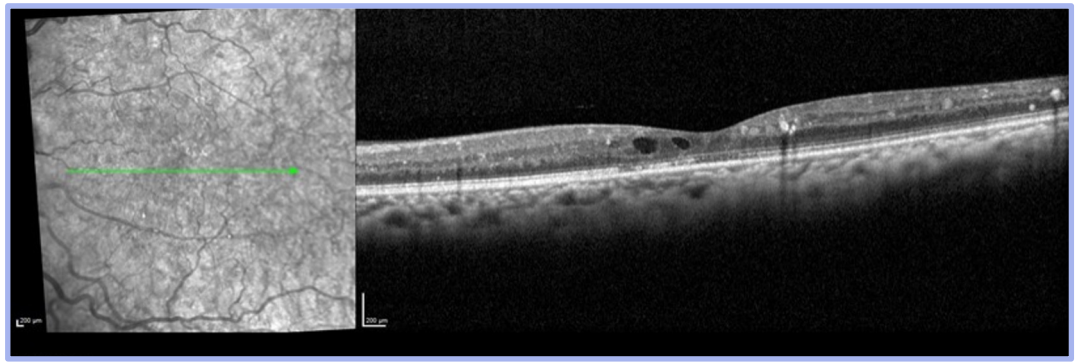
**8 Weeks After Faricimab #4**
21 December 2022

**BCVA:** 20/25 **CST:** 284 µm



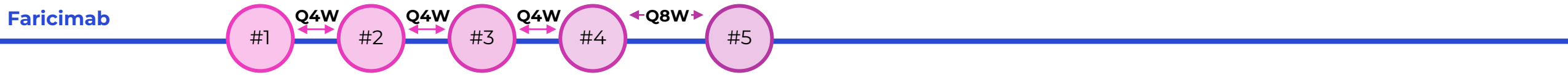
**8 Weeks After Faricimab #5**
15 February 2023

**BCVA:** 20/25 **CST:** 249 µm



Faricimab #5 given

No treatment given, and patient extended to Q16W for faricimab #6



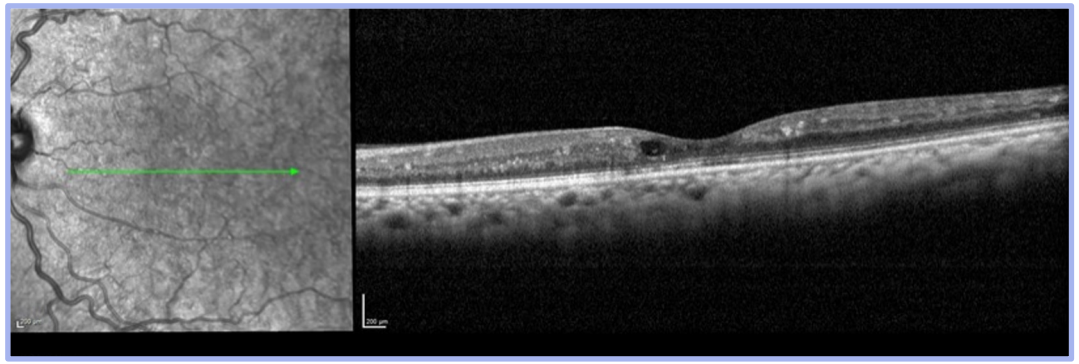

BCVA, best-corrected visual acuity; CST, central subfield thickness; QXW, every X weeks.

# Case Study: DME In Left Eye Treated With Faricimab Q16W

**Left Eye**

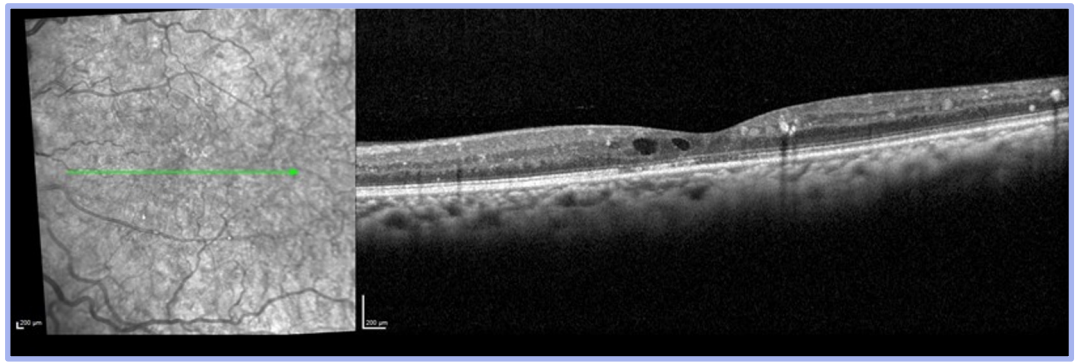
**16 Weeks After Faricimab #5**
12 April 2023

**BCVA:** 20/25 **CST:** 236 µm



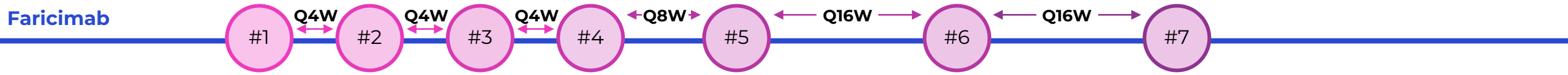
**16 Weeks After Faricimab #6**
02 August 2023

**BCVA:** 20/25 **CST:** 231 µm



Faricimab #6 given

Faricimab #7 given, and patient told to follow up in 16 weeks



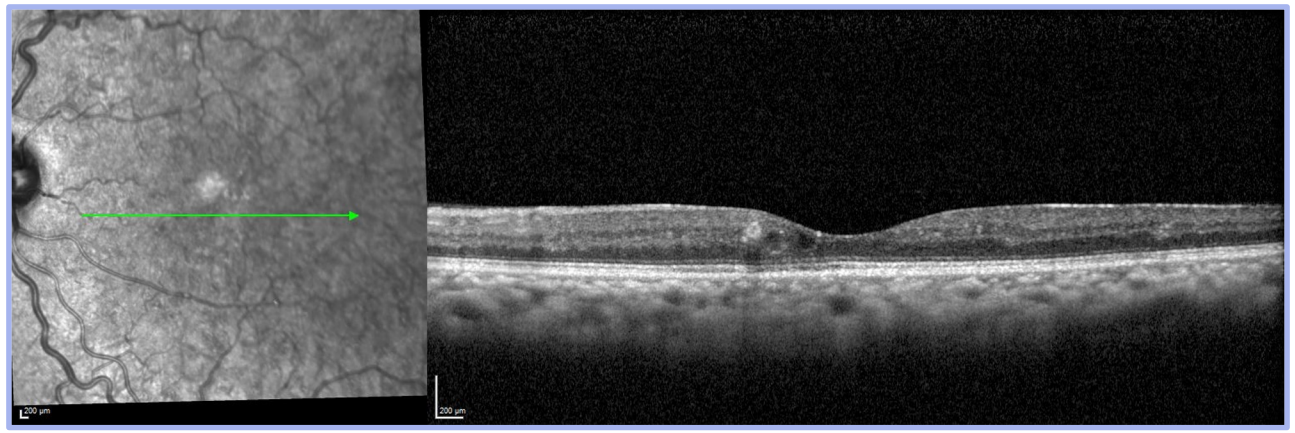

BCVA, best-corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; QXW, every X weeks.

# Case Study: Patient Received Injection At Q28W After Missing Q16W Follow-Up

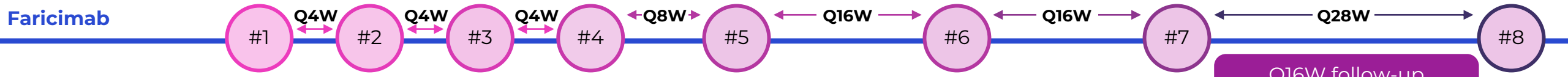
**Left Eye**

**28 Weeks After Faricimab #7**
14 February 2024

**BCVA:** 20/25 **CST:** 237 µm



Faricimab #8 given



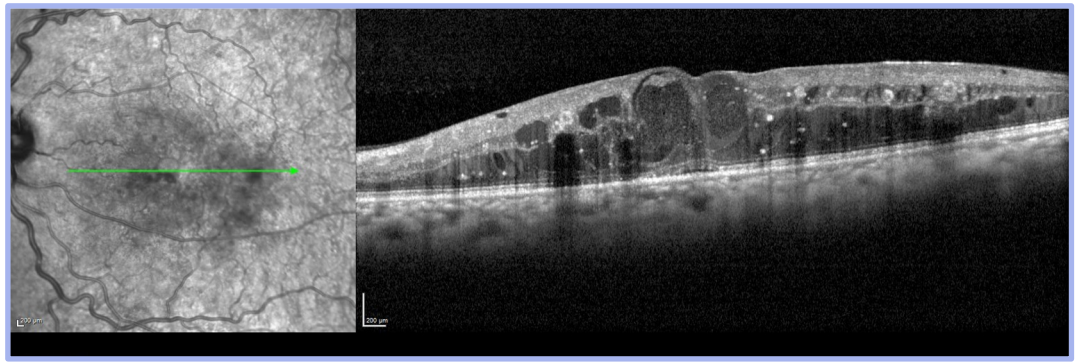

Q16W follow-up missed, and patient returned at Q28W

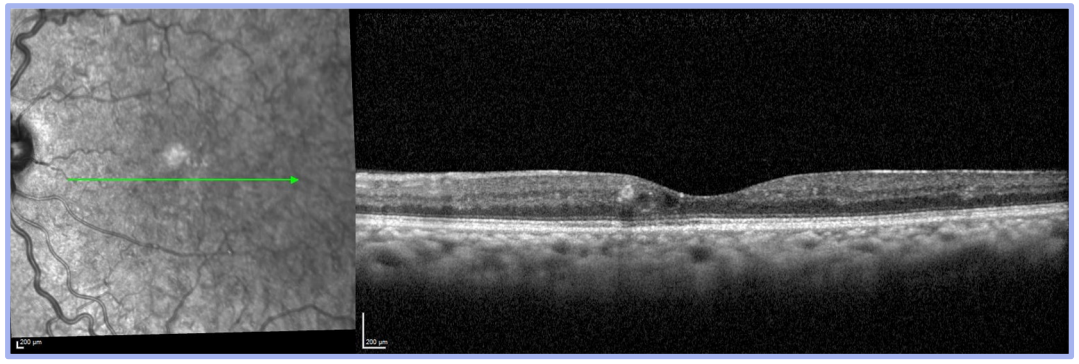
BCVA, best-corrected visual acuity; CST, central subfield thickness; QXM: every X months; QXW, every X weeks.

# Case Study: Summary And Discussion

**Left Eye**

| Return To Clinic After 10 months | 28 Weeks After Faricimab #7 |
|---|---|
| **BCVA:** 20/80 | **BCVA:** 20/25 |
| **CST:** 625 µm | **CST:** 237 µm |





Patient with treatment-naïve DME: Rapid improvements in vision and central DME, leading to **extension** of faricimab treatment

No serious ocular adverse drug reactions were observed/reported in the treated eye

BCVA, best-corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; QXM: every 6 months; QXW, every X weeks.

# Take Home Messages

Trial data demonstrate dual pathway inhibition leads to **robust drying** through 2 years

**Greater drying** in the head-to-head period with faricimab vs aflibercept 2mg

Drying outcomes in the **real world reflect the results in clinical trials**

# Time for Some Questions!

# Which type of meat is traditionally used in IKEA's famous Swedish meatballs?

Roche

A Chicken

B Beef and pork

C Lamb

D Turkey


VEERAL SHETH

PATRICIA UDAONDO

RAJ MUKHERJEE

# Which type of meat is traditionally used in IKEA's famous Swedish meatballs?

Roche

A Chicken

B Beef and pork

C Lamb

D Turkey

50:50

VEERAL SHETH

PATRICIA UDAONDO

RAJ MUKHERJEE

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50:50

VEERAL SHETH

PATRICIA UDAONDO

RAJ MUKHERJEE

Roche

# Which type of meat is traditionally used in IKEA's famous Swedish meatballs?


B Beef and pork

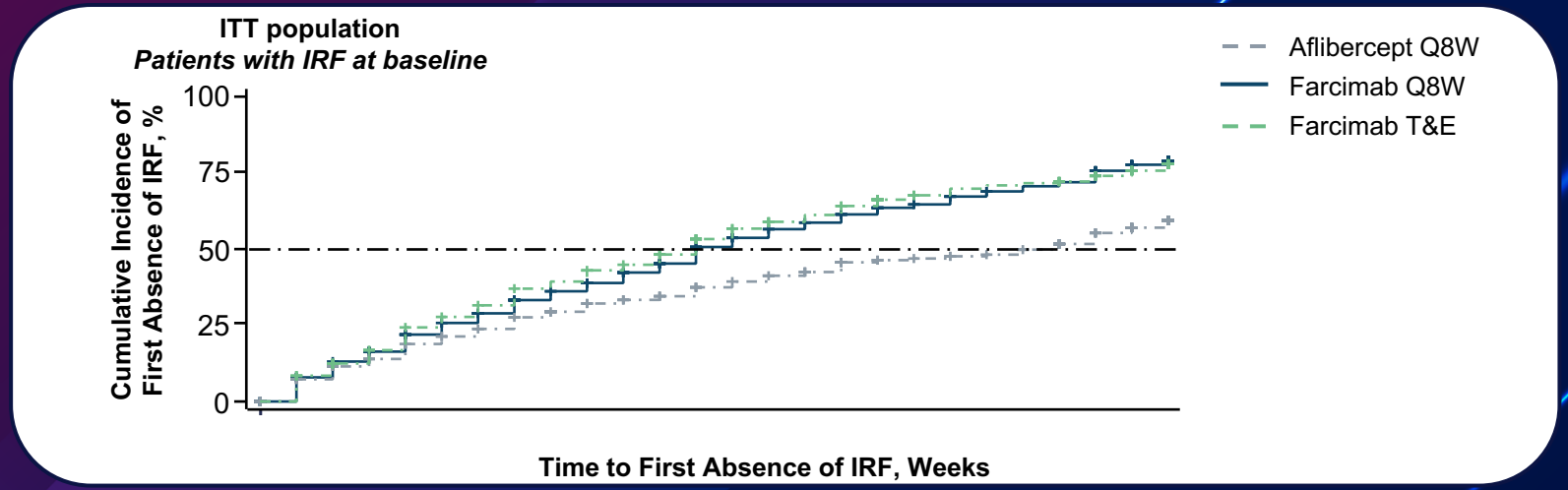
D Turkey

VEERAL SHETH

PATRICIA UDAONDO

RAJ MUKHERJEE

# How many weeks faster did faricimab achieve the median first absence of IRF vs aflibercept 2 mg in the time-to-event analysis below?




**A** 35 Weeks

**B** 40 Weeks

**C** 7 Weeks

**D** 24 Weeks

50:50

Manoharan N *et al*. ARVO 2024.

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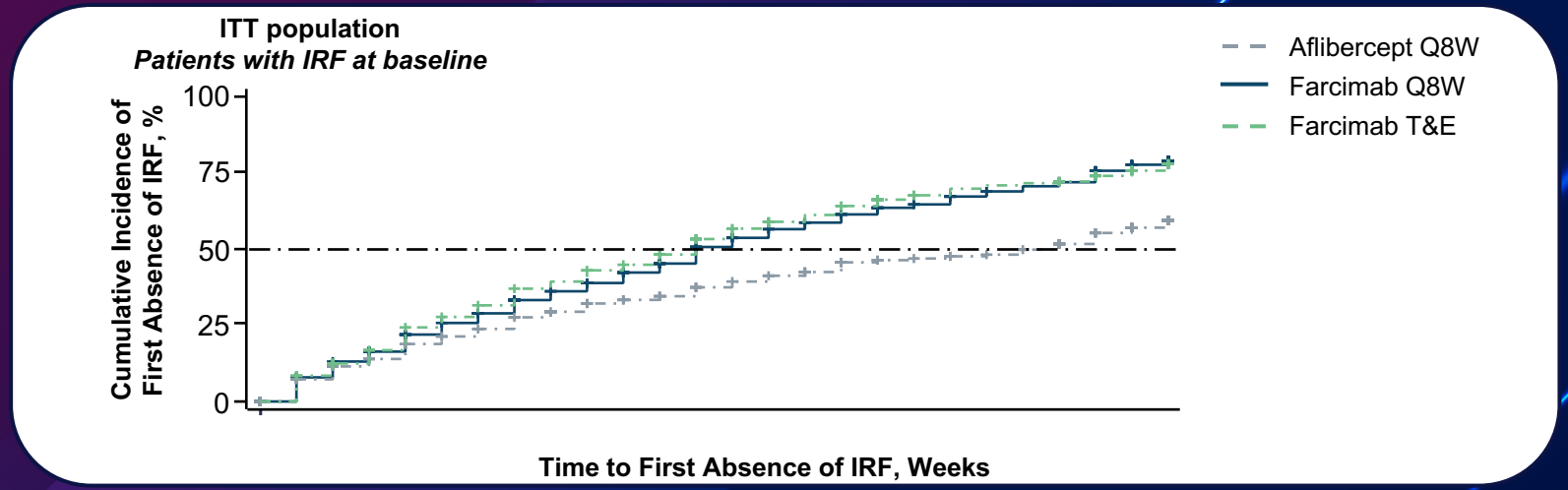


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Manoharan N *et al*. ARVO 2024.

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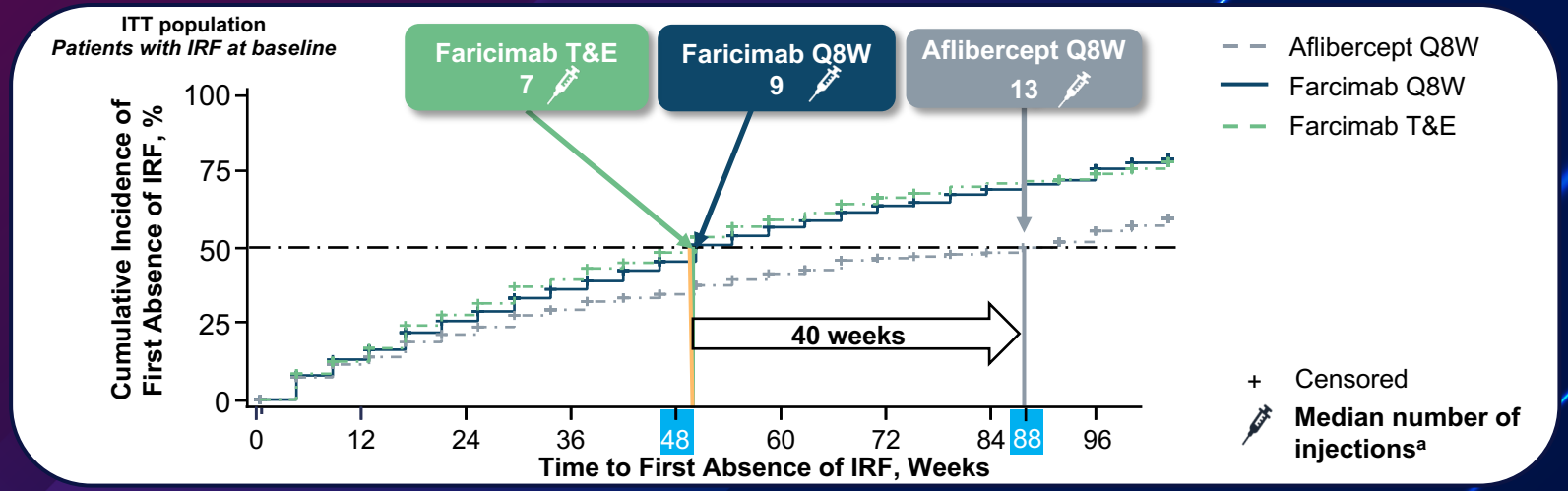



A 35 Weeks

B 40 Weeks

C 7 Weeks

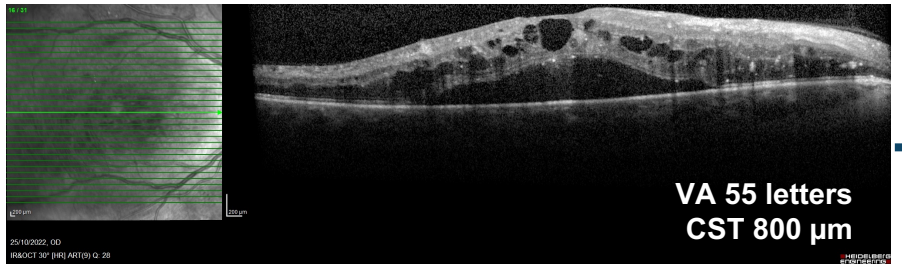
D 24 Weeks

Manoharan N *et al*. ARVO 2024.

VEERAL SHETH PATRICIA UDAONDO RAJ MUKHERJEE

# How many injections of faricimab did it take for the right eye of this patient with DME to go from image A to image B?

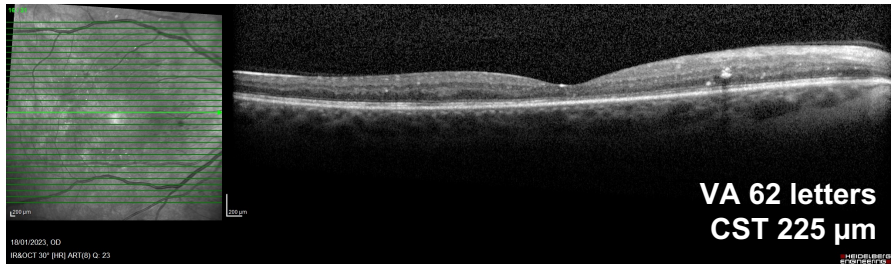
A




Baseline

?

B




A 1

B 2

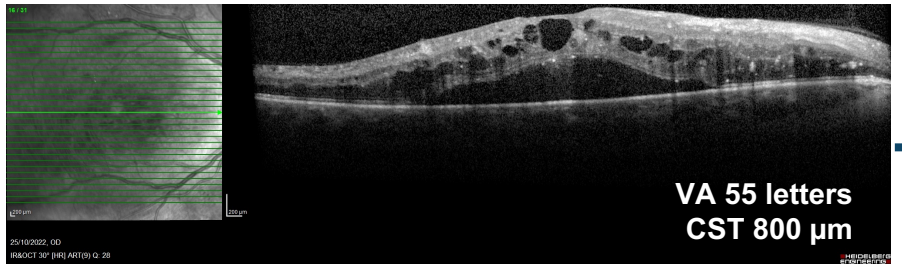
C 3

D 4

50:50

# How many injections of faricimab did it take for the right eye of this patient with DME to go from image A to image B?

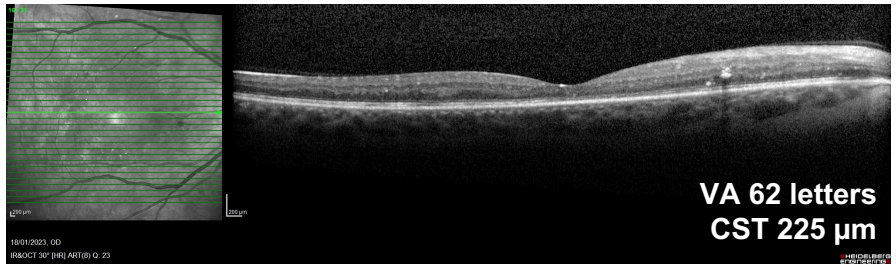
A




Baseline

1

B




A 1

B 2

C 3

D 4

50:50

# Round 2

Roche

| | | |
|---|---|---|
| 2 / 3 |  | PATRICIA UDAONDO |
| 1 / 3 |  | RAJ MUKHERJEE |
| 1 / 3 |  | VEERAL SHETH |

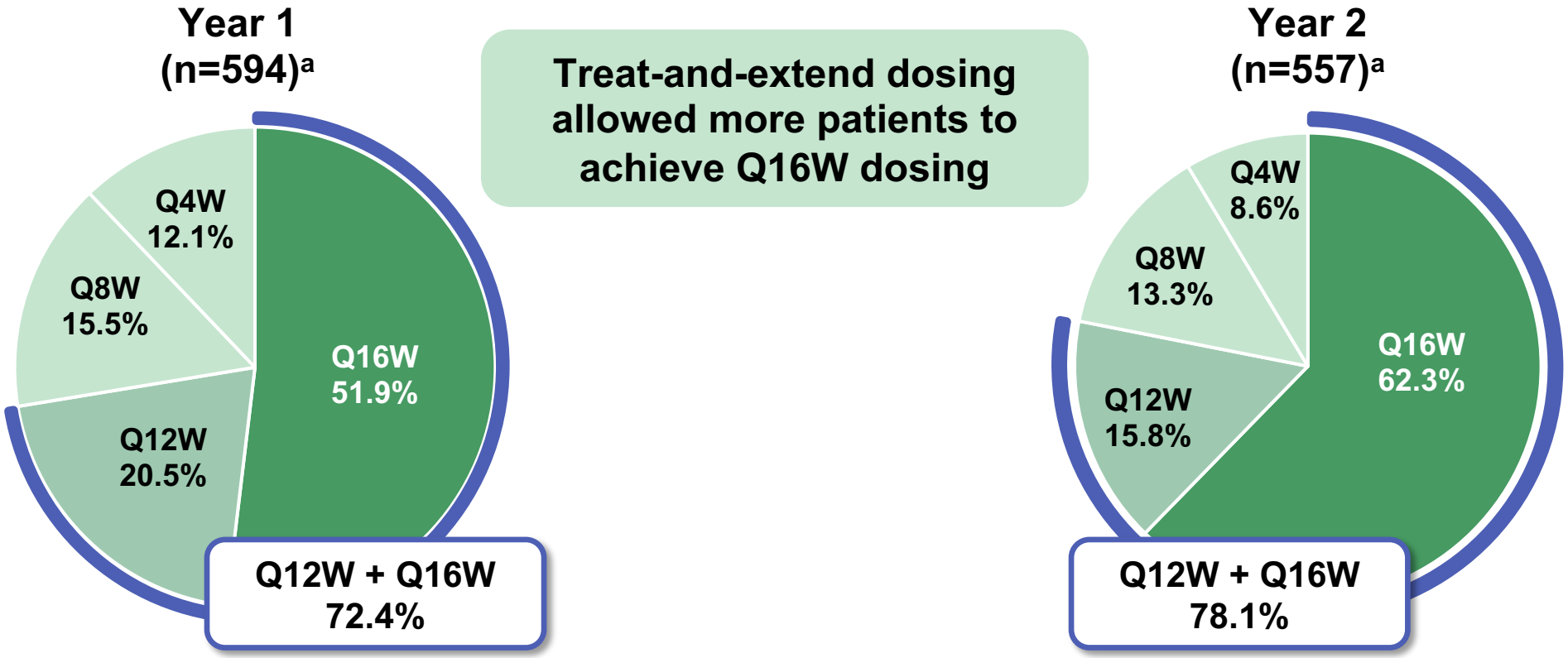
# Durability: Reducing Treatment Burden


## Raj Mukherjee

Consultant Ophthalmologist, Leeds Teaching Hospitals NHS Trust

# ~80% Of Faricimab-Treated Patients Achieved ≥Q12W Dosing At The End Of The Second Year[1]

## YOSEMITE/RHINE pooled

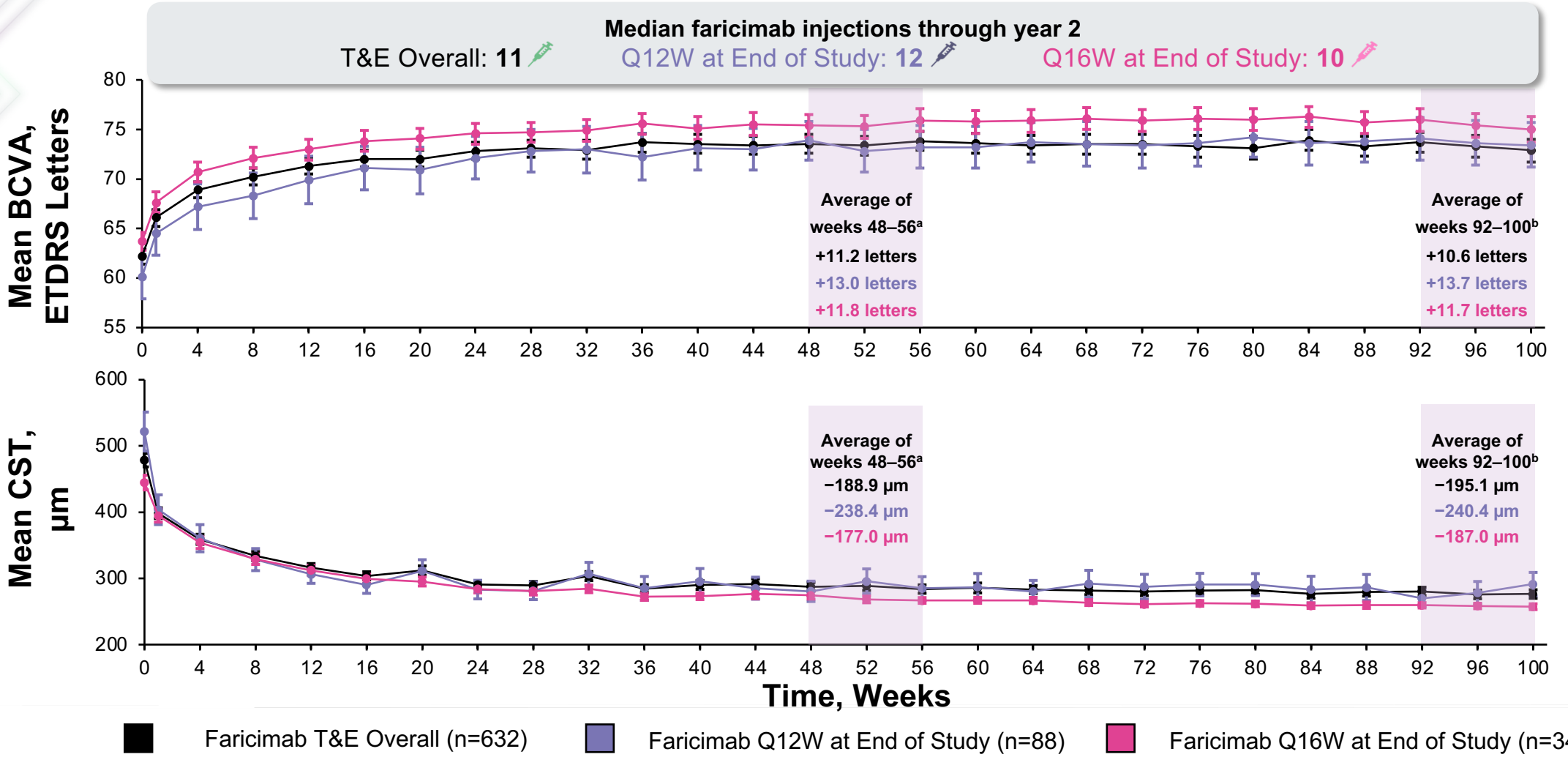



[a]Proportion of patients in the pooled faricimab T&E arms on Q4W, Q8W, Q12W, or Q16W dosing at Week 52 (Year 1) and Week 96 (Year 2), among those who had not discontinued the study at that visit. Treatment interval at a given visit is defined as the treatment interval decision made at that visit. Interval at Week 52 and 96 is calculated using data up to Week 52 and 96, respectively. QXW, every X weeks; T&E, treat-and-extend.

1. Lim JI. Angiogenesis, Exudation, and Degeneration 2024 Virtual Congress.

# Robust And Stable Vision And CST Improvements Through 2 Years In Patients On Q12W Or Q16W Dosing At Week 96[1]

## YOSEMITE/RHINE pooled post hoc analysis




[a]Descriptive summary of mean change from baseline at 1 year, averaged over Weeks 48, 52 and 56. [b]Descriptive summary of mean change from baseline at 2 years, averaged over Weeks 92, 96 and 100.
BCVA, best corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; QXW, every X weeks; T&E, treat-and-extend. 1. Figueroa MS *et al.* Retina World Congress. 2023.

# Faricimab Outcomes In Treatment-Naïve Patients In The Leeds DME Service

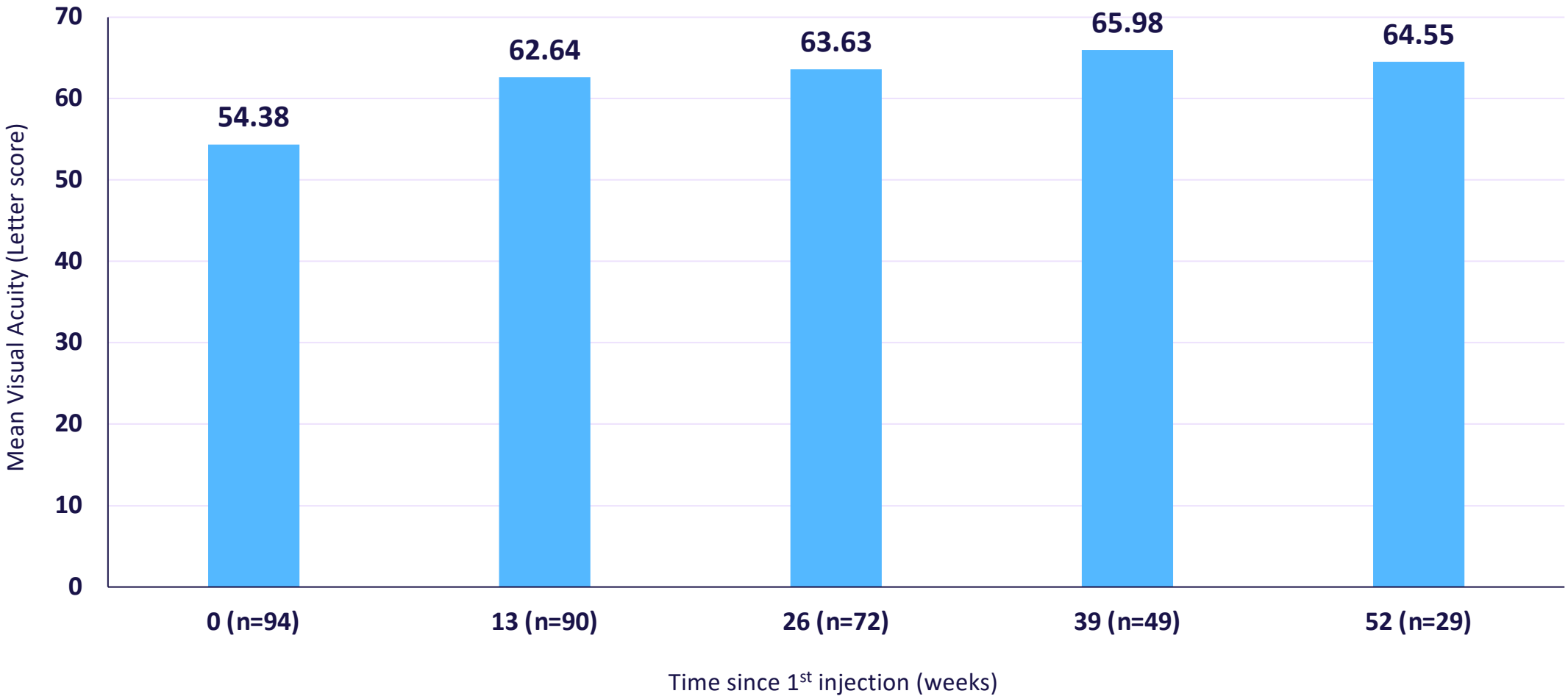
# DME Protocol At Leeds Teaching Hospital[1]

- First treatment on the day of presentation
  - Vision, IOP, OCT, Optos
- 4 loading doses 4 weeks apart
  - No imaging
- 5th appointment 8 weeks after 4 loading
  - Face-to-face appointment and imaging every visit
- Treat-and-extend
  - Extend by 4 weeks and reduce by 2 weeks
  - CST worsening due to fovea involving oedema AND vision worsening by >5 letters

Faricimab experience since August 2022: **151 patients, 216 eyes, 1,227 injections**

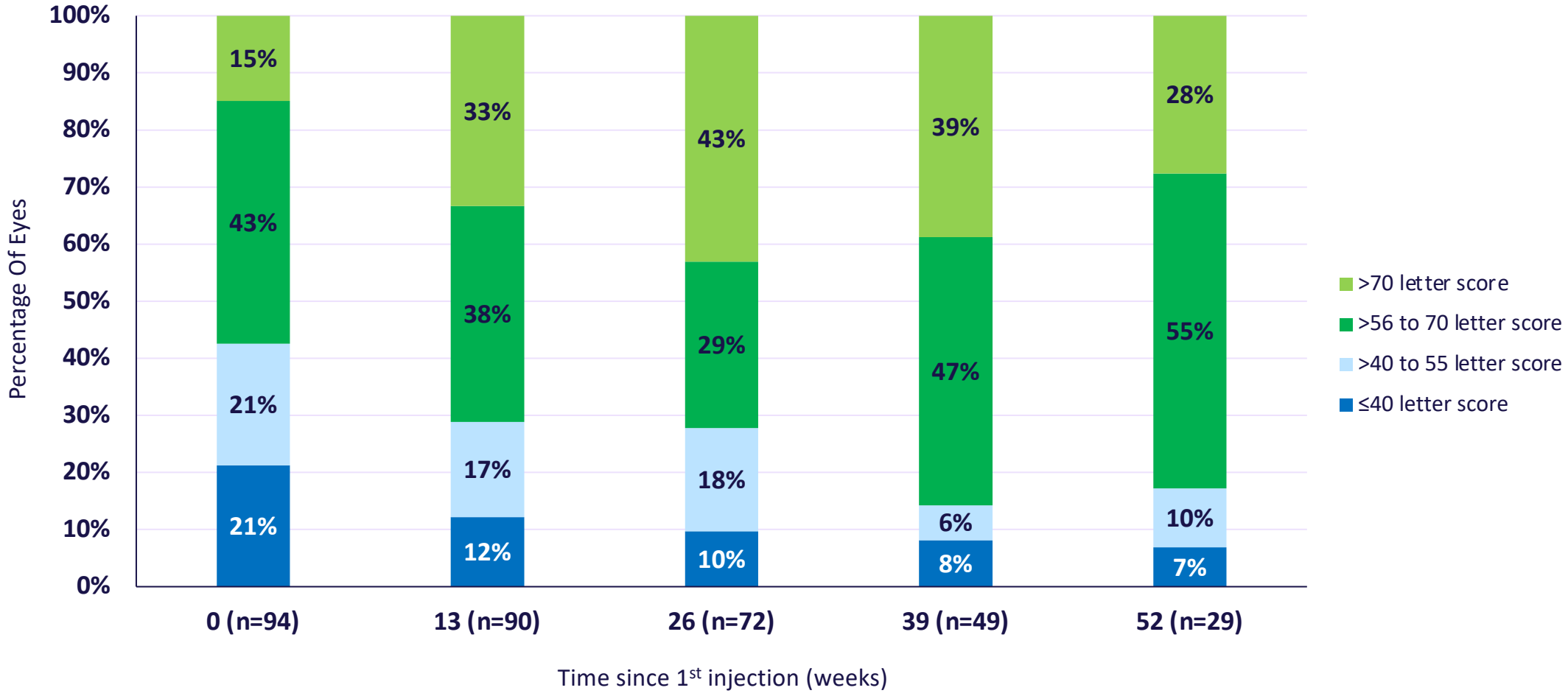
CST, central subfield thickness; DME, diabetic macular edema; IOP, intraocular pressure; OCT, optical coherence tomography. 1. Leeds Teaching Hospital Cohort Data.

# Visual Acuity Outcomes: >10 Letter Improvement At 1 Year[1]



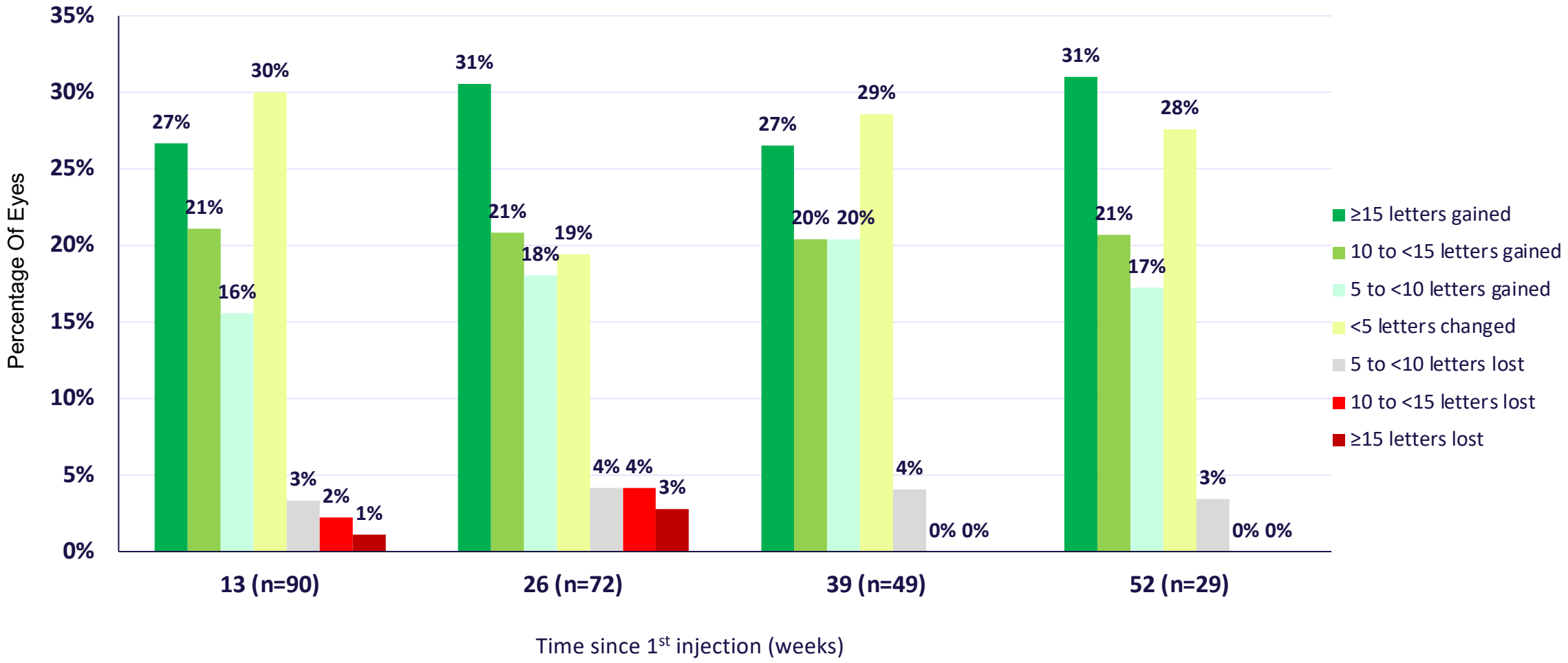

1. Leeds Teaching Hospital Cohort Data.

# Visual Acuity Outcomes: % Of Patients With >55 Letters Progressively Improved While Those With <40 Letters Vision Reduced[1]



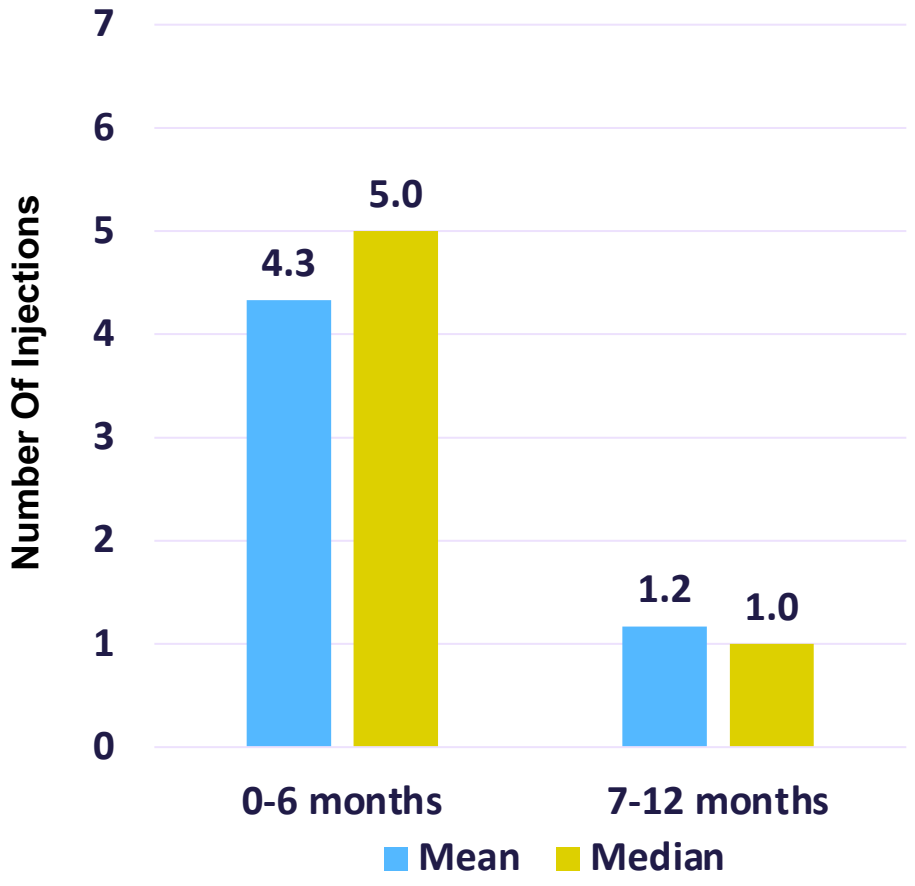

1. Leeds Teaching Hospital Cohort Data.

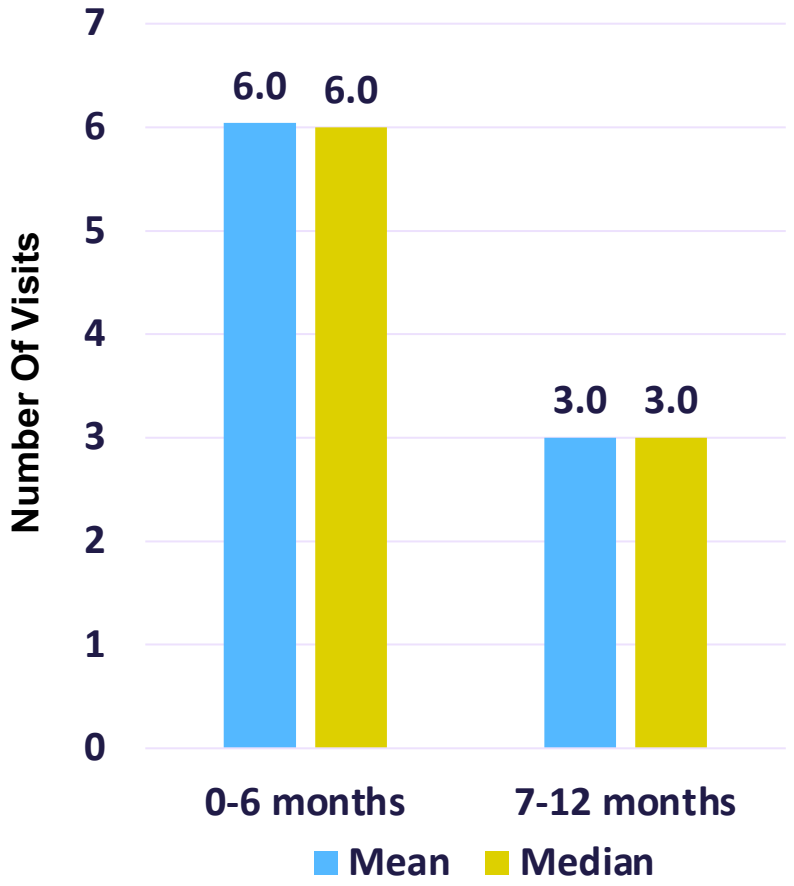
# Visual Acuity Outcomes: Within The First Year, ~68% Patients Gained ≥5 Letters And ~28% Remained Stable (<5 Letter Gain/Loss)[1]




1. Leeds Teaching Hospital Cohort Data.

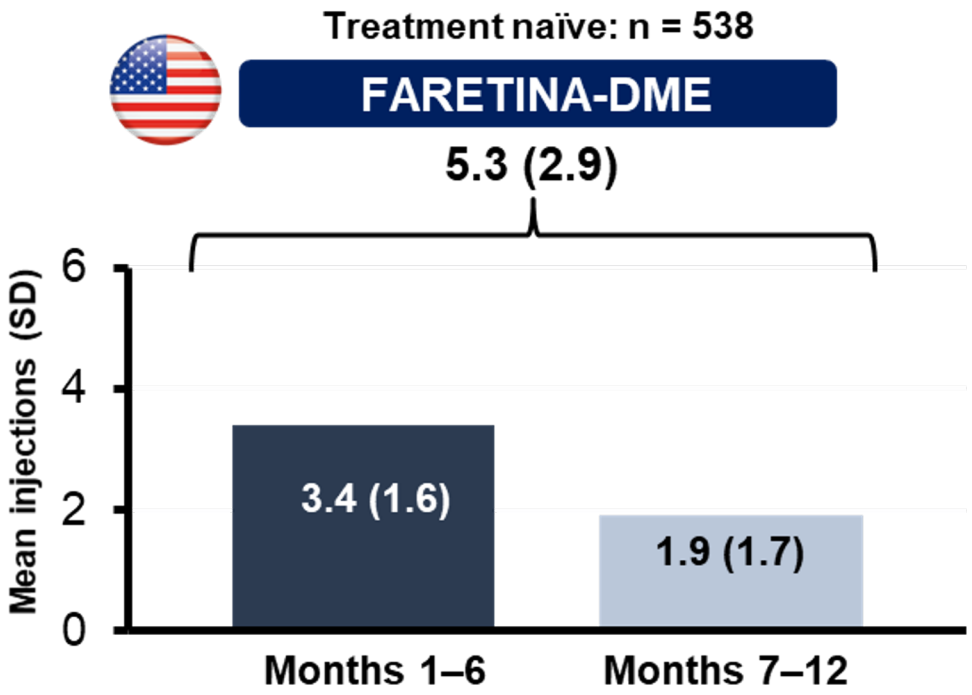
# Visual Acuity Outcomes: Number Of Injections And Number Of Visits[1]

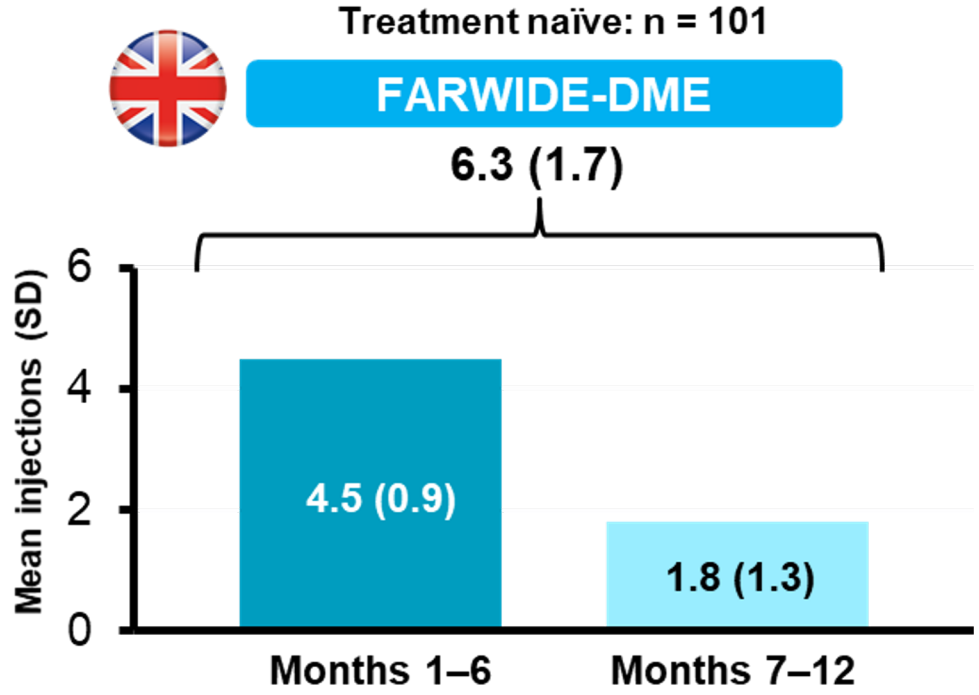



1. Leeds Teaching Hospital Cohort Data.

# RWD: Mean Injections In Months 7–12 Of Faricimab Treatment Were Lower Than Months 1–6 In Eyes With DME[1]

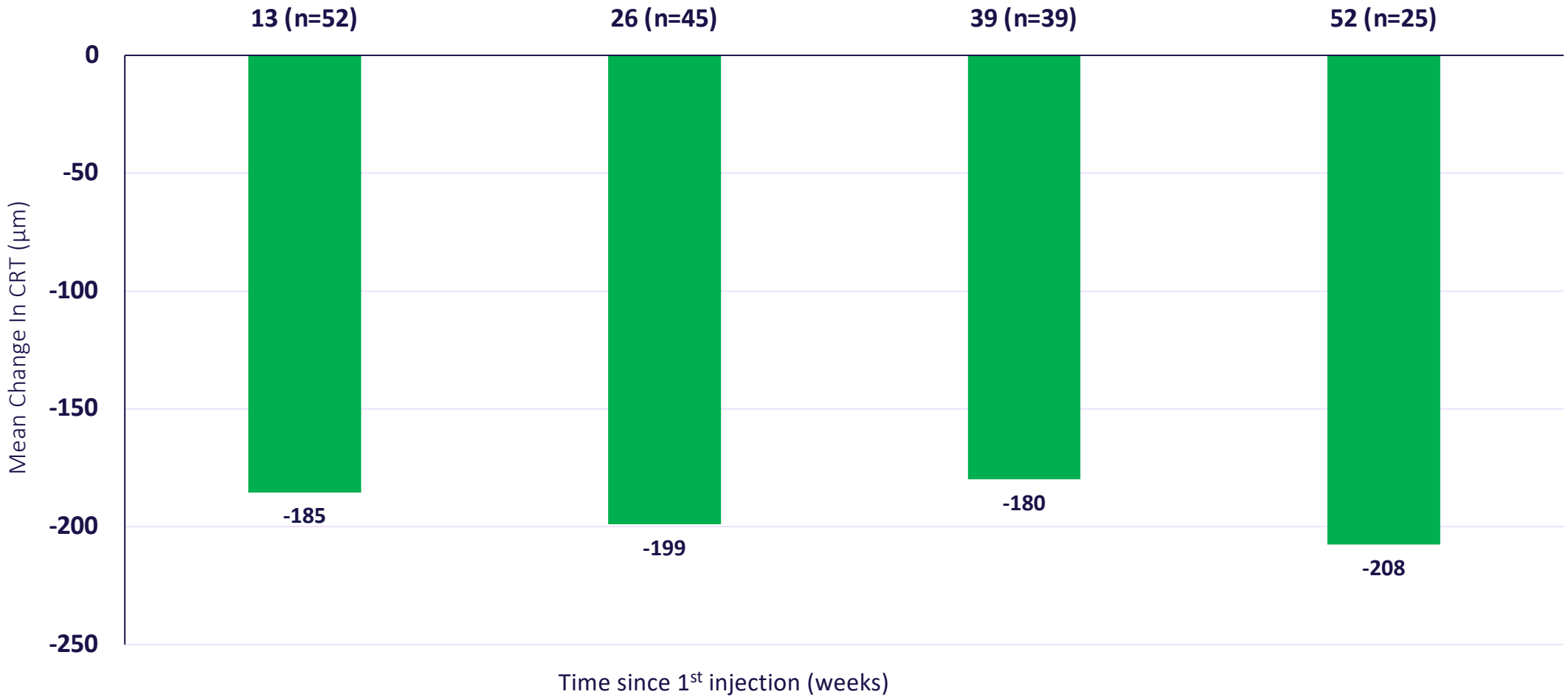



In **YOSEMITE/RHINE,** mean injections (SD) through week 28 and weeks 32–56 were **5.8 (1.2)** and **2.9 (1.5)**, respectively
**Fewer injections during the second 6 months** of faricimab treatment indicates extension of treatment intervals

DME, diabetic macular edema; RWD, real world data; SD, standard deviation. 1. Singh RP. BRAVS 2024.

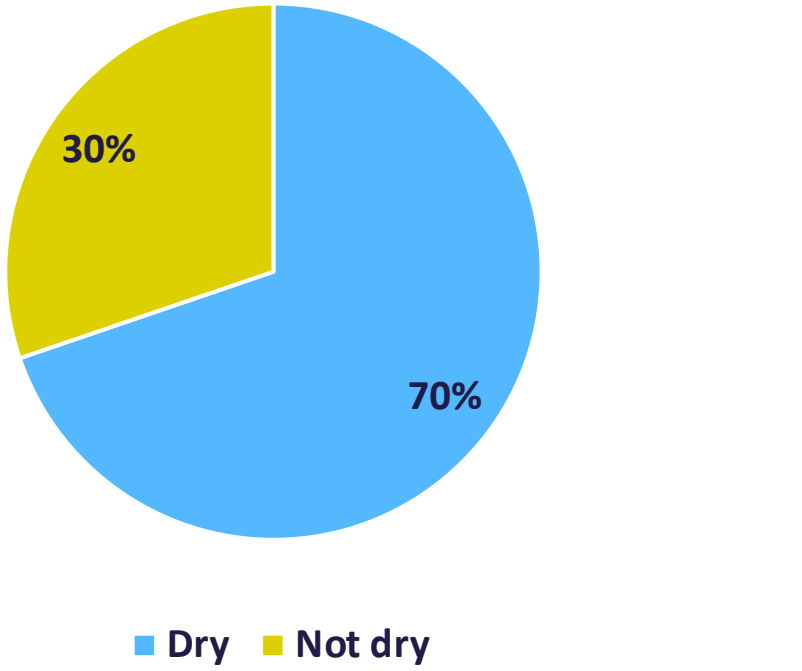
# Anatomical Outcomes: ~200 Microns Reduction In CRT After 1 Year



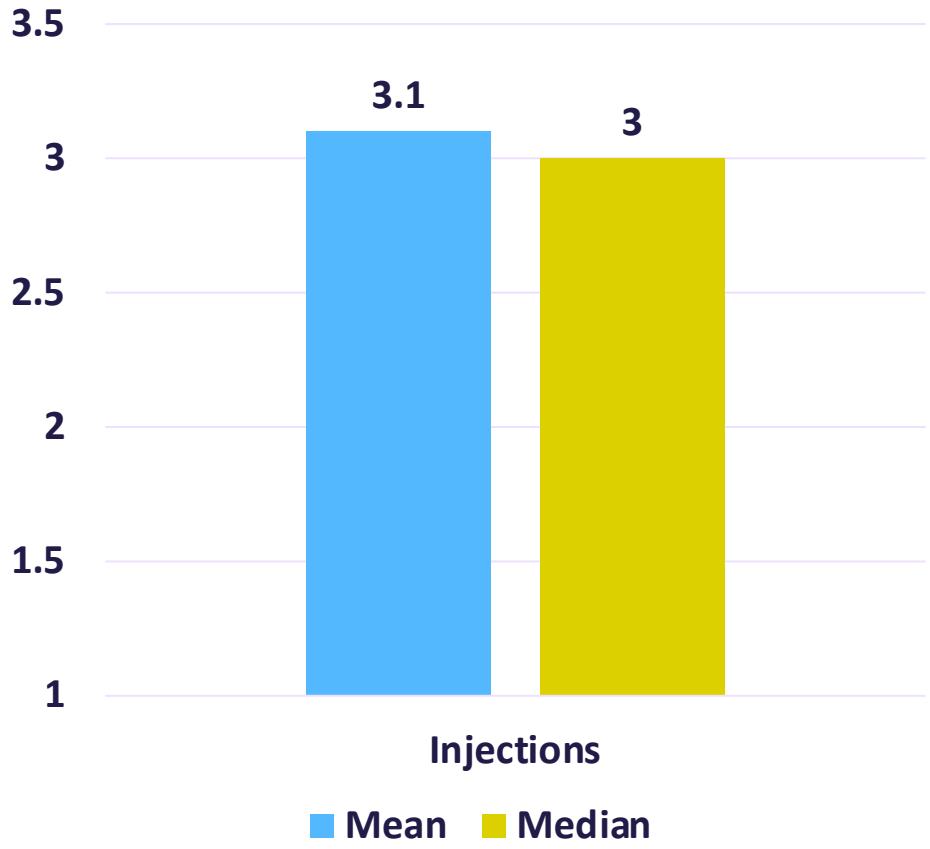

CRT, central retinal thickness. 1. Leeds Teaching Hospital Cohort Data.

# Drying: No Fluid Or Exudate In Central 1 mm OCT

## Proportion of dry patients (n=87)




## Average number of injections required for drying (n=87)




OCT, optical coherence tomography. 1. Leeds Teaching Hospital Cohort Data.

# Conclusions

**Treatment with faricimab led to:**

1. ~10 letter improvement after 1 year
2. ~200 microns reduction in the central subfoveal thickness at 1 year
3. 70% patients are dry on average after 3 injections

1. Leeds Teaching Hospital Cohort Data.

# Take Home Messages

**Drying and durability are linked**; you cannot have one without the other

Trial data demonstrate **extended durability of faricimab**, without compromising outcomes

Durability outcomes in the **real world reflect the results in clinical trials**

# Time for Some Questions!

Roche

# Which iconic Swedish building has hosted the Nobel Prize banquet every year since 1930?

A The Royal Palace

B Stockholm City Hall

C The Vasa Museum

D Drottningholm Palace


VEERAL SHETH PATRICIA UDAONDO RAJ MUKHERJEE

Roche

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Roche

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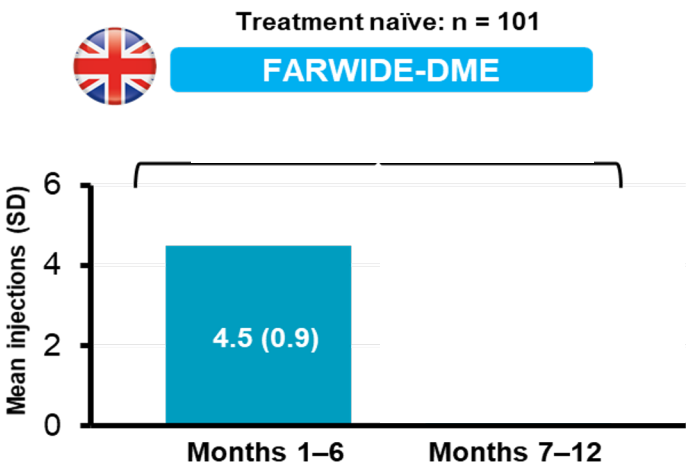
50:50

VEERAL SHETH PATRICIA UDAONDO RAJ MUKHERJEE

# In FARWIDE, for treatment-naïve patients, what was the mean number of injections in Months 7–12?




**A** 3.9

**B** 2.1

**C** 1.8

**D** None of the above

50:50

Singh RP. BRAVS 2024

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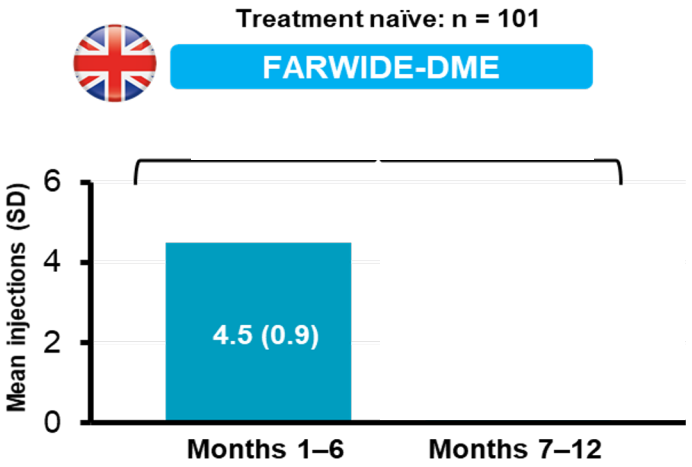


**A** 3.9

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50:50

Singh RP. BRAVS 2024

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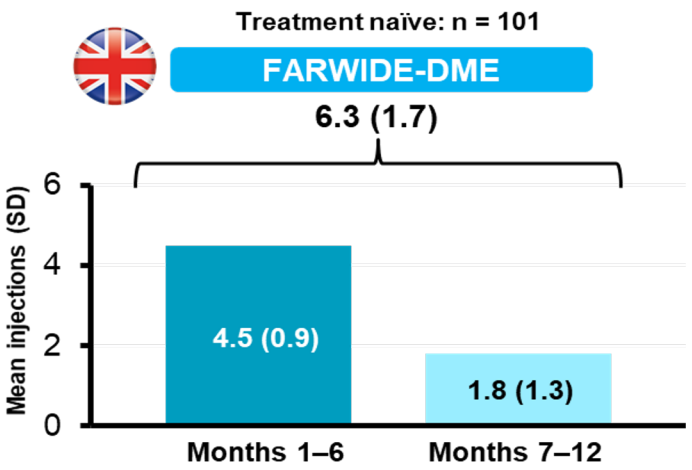



A 3.9

B 2.1

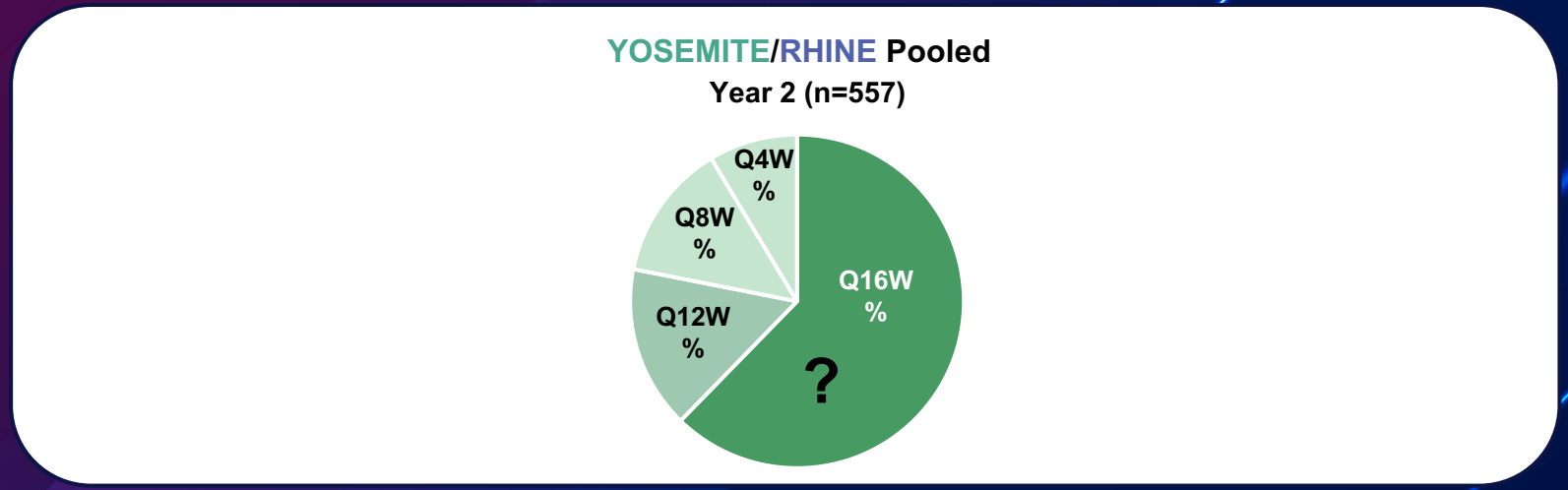
C 1.8

D None of the above

50:50

Singh RP. BRAVS 2024

# In YOSEMITE/RHINE, what percentage of patients in the faricimab T&E arm achieved Q16W dosing at the end of the 2-year study?




**A** 62.3%

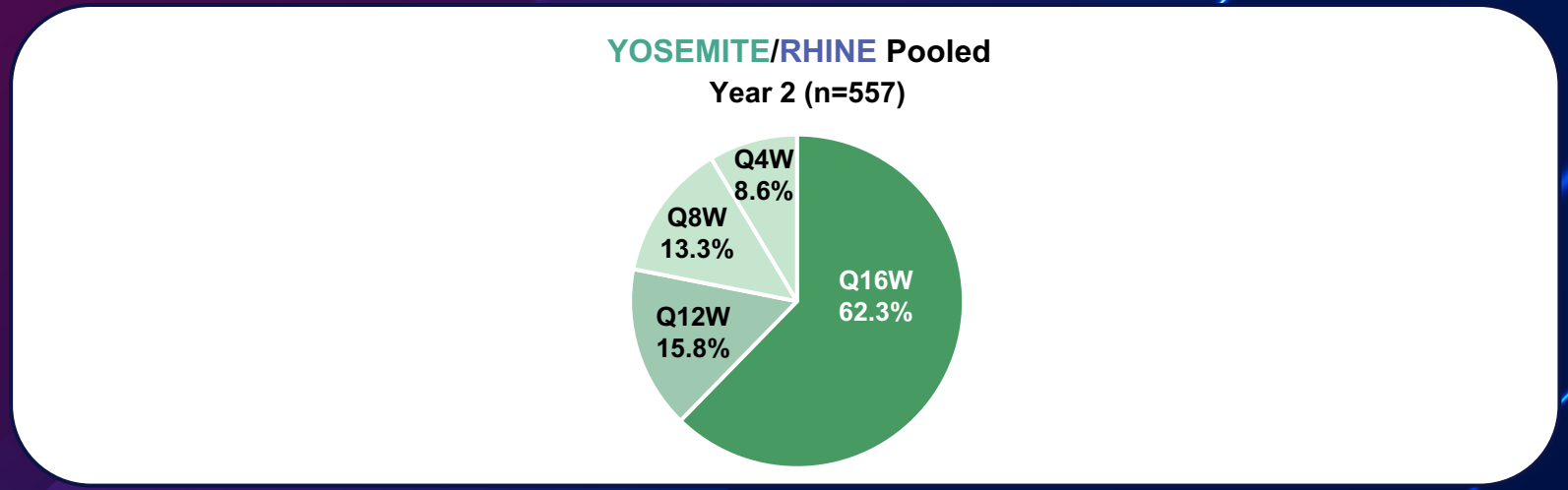
**B** 60.1%

**C** 67.8%

**D** 72.1%

Lim JI. Angiogenesis, Exudation, and Degeneration 2024 Virtual Congress.

# In YOSEMITE/RHINE, what percentage of patients in the faricimab T&E arm achieved Q16W dosing at the end of the 2-year study?




**A** 62.3%

**B** 60.1%

**C** 67.8%

**D** 72.1%

Lim JI. Angiogenesis, Exudation, and Degeneration 2024 Virtual Congress.

# And the WINNER is...

1

PATRICIA UDAONDO

2

RAJ MUKHERJEE

2

VEERAL SHETH

# Closing Remarks

## Arshad Khanani (Chair)

Director of Clinical Research, Sierra Eye Associates;
Clinical Professor, University of Nevada, Reno School of Medicine,
Reno, NV, USA

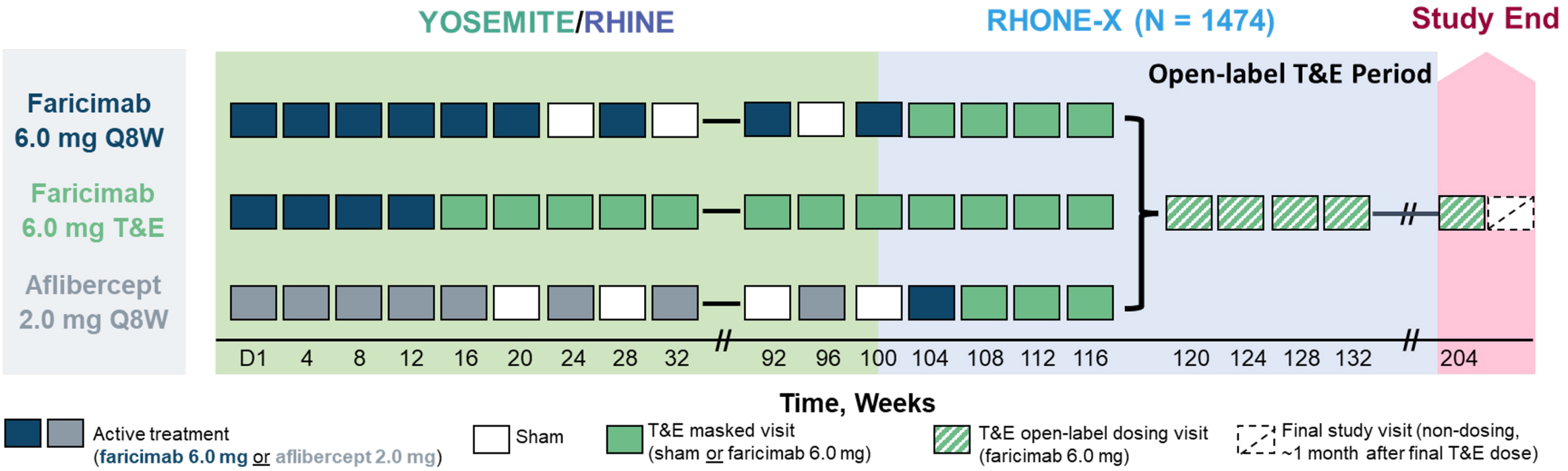
# RHONE-X Extension Trial Assessed The Long-Term Safety And Efficacy Of Faricimab Treat-And-Extend In Patients With DME

**Phase 3, Multicenter, Open-Label, Long-Term Extension Trial**

- Patients with DME who completed either YOSEMITE or RHINE without discontinuation of study treatment were eligible to be included
- Patients were followed for an additional 2 years to assess the safety and efficacy of faricimab over 4 years

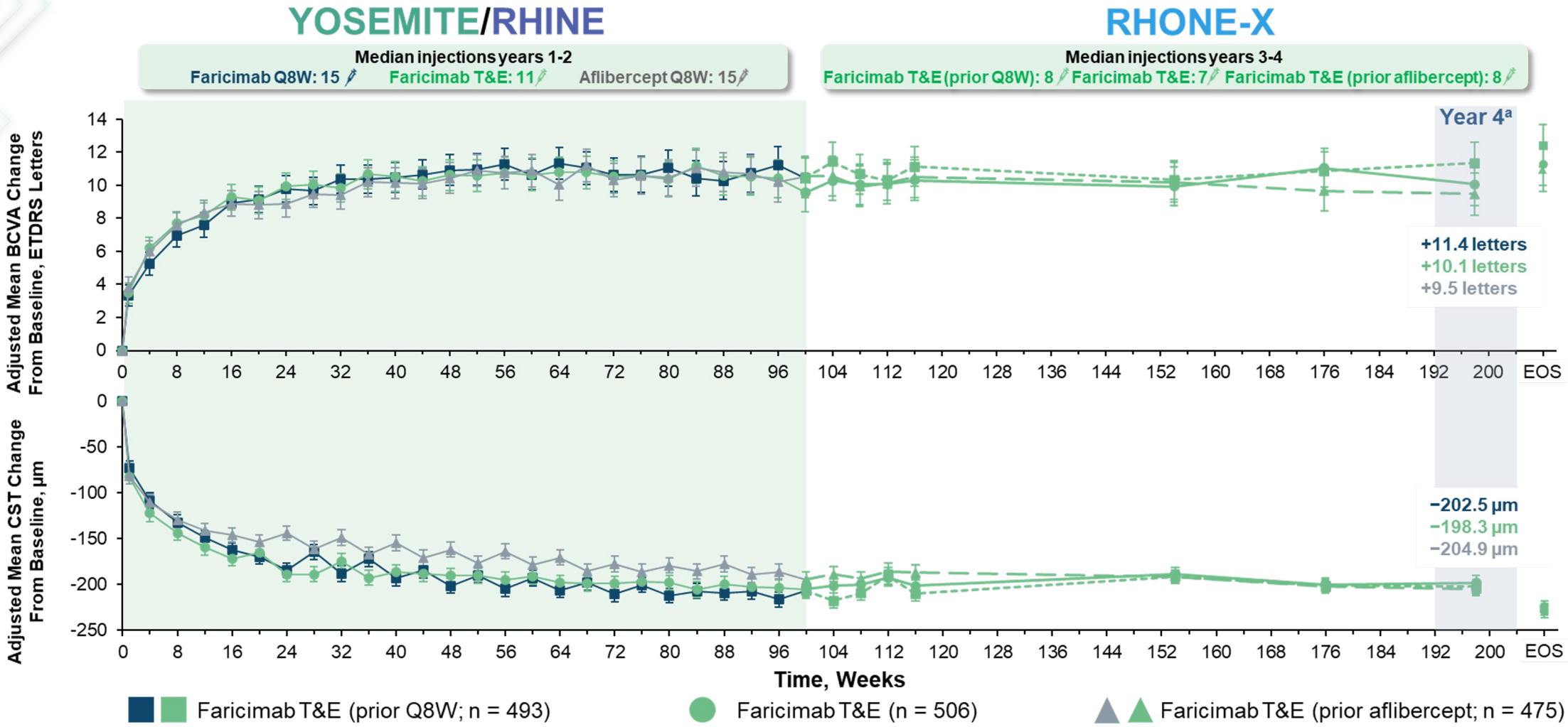
**Faricimab Treat & Extend In RHONE-X**

- Patients in RHONE-X attended monthly visits during the first 16 weeks (masked period) and subsequently only attended at T&E dosing visits (open label period)
- All patients received faricimab T&E up to Q16W



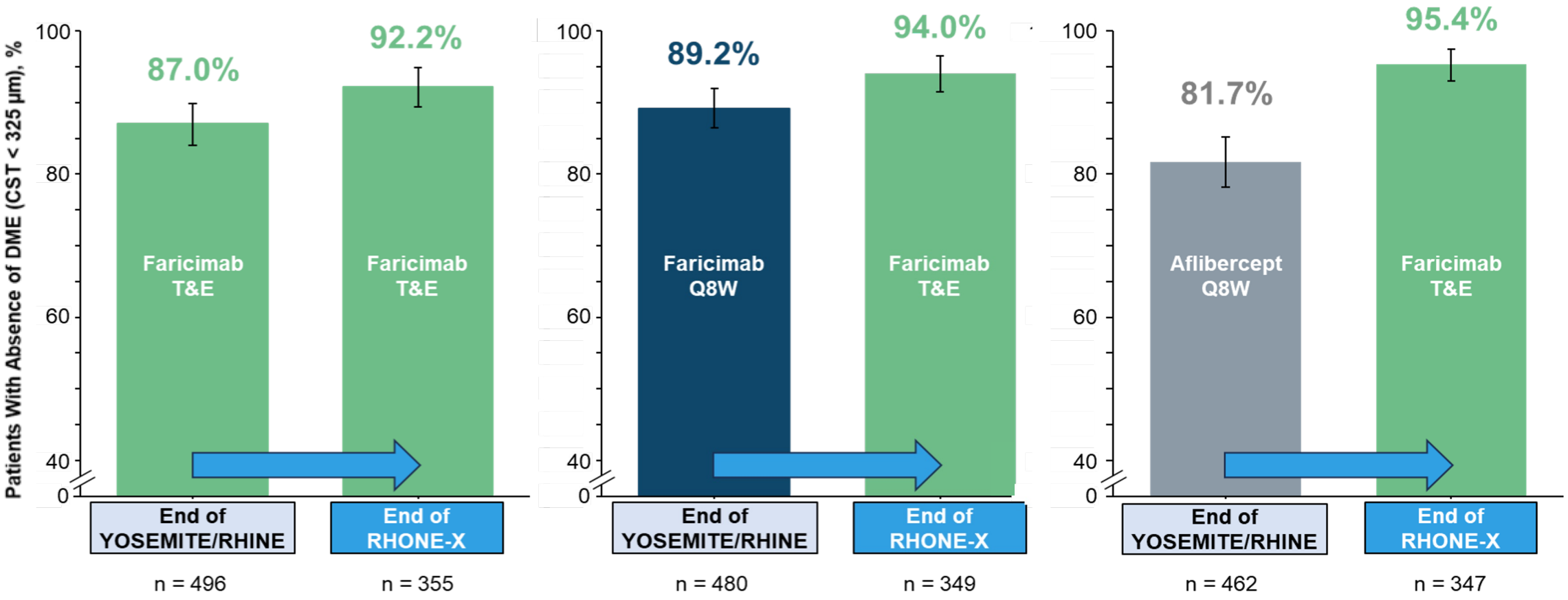

Personalized T&E–based dosing regimen: stable CST + BCVA, dosing extended (by 4 weeks, max Q16W); worsening CST ± BCVA, dosing reduced by 4 or 8 weeks, min Q4W); extension or reduction criteria not met: dosing maintained. Faricimab T&E regimen started at Week 100/Day 1 of RHONE-X for faricimab Q8W and aflibercept Q8W but not all patients received faricimab at Week 100. BCVA, best-corrected visual acuity; CST, central subfield thickness; D, day; DME, diabetic macular edema; QXW, every X weeks; T&E, treat-and-extend. 1. Khanani AM *et al.* ASRS 2024.

# Robust Vision Gains And Improved CST Achieved During YOSEMITE/RHINE Were Maintained In RHONE-X With Faricimab Up To Q16W Dosing[1]



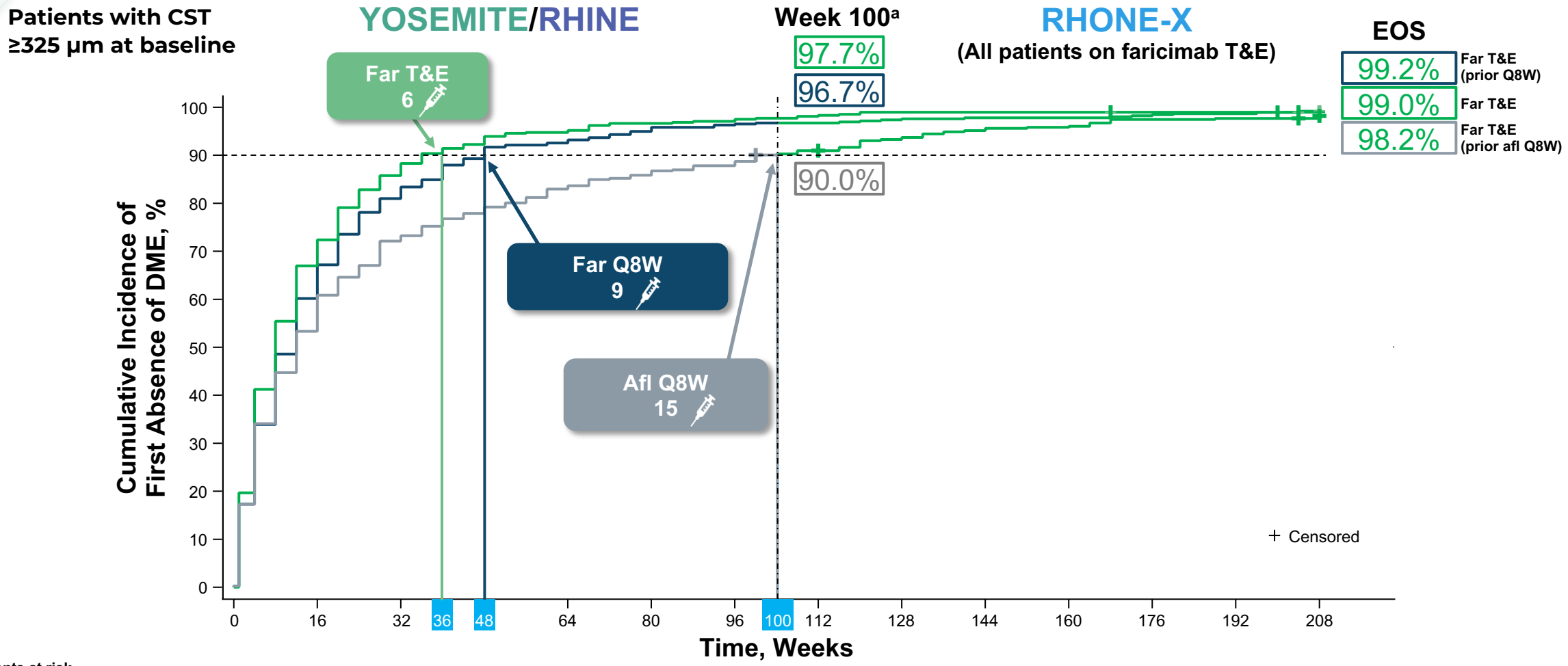

Faricimab T&E regimen started at Week 100/Day 1 of RHONE-X for faricimab Q8W and aflibercept Q8W but not all patients received faricimab at Week 100. Estimates for year 3 and 3.5 are averaged over Weeks 144 to 164 and 168 to 188, respectively. [a]Adjusted mean change from baseline at Year 4 of RHONE-X, averaged over Weeks 192 to 204. EOS minimum of 28 days after the final faricimab dose. Analysis of Covariance model was adjusted for parent study treatment group, visit, visit-by-treatment group interaction, baseline BCVA (continuous) or baseline CST (continuous) as applicable, baseline BCVA (<64 vs ≥64 ETDRS letters), prior intravitreal anti-VEGF therapy (yes vs no), region (US and Canada, and the rest of the world). 95% CI error bars are shown. BCVA, best-corrected visual acuity; CST, central subfield thickness; EOS, end of study; ETDRS, Early Treatment Diabetic Retinopathy Study; Q8W, every 8 weeks; Q16W, every 16 weeks; T&E, treat & extend; VEGF, vascular endothelial growth factor. 1. Khanani AM *et al.* ASRS 2024.

# Absence Of DME Was Achieved By >90% Of Patients By The End Of RHONE-X Regardless Of Prior Treatment Arm[1]




Faricimab T&E regimen started at Week 100/Day 1 of RHONE-X for faricimab Q8W and aflibercept Q8W but not all patients received faricimab at Week 100. Weighted estimates were based on CMH test stratified by baseline BCVA score (<64 letters vs ≥64 letters), prior intravitreal anti-VEGF therapy (yes vs no), and region (U.S. and Canada vs the rest of the world). Missing data were not imputed. Estimates <0% or >100% were imputed as 0% or 100% respectively. 95% CI error bars are shown. AE, adverse event; BCVA, best-corrected visual acuity; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; CST, central subfield thickness; DME, diabetic macular edema; QXW, every X weeks; T&E, treat-and-extend; VEGF, vascular endothelial growth factor. 1. Khanani AM *et al.* ASRS 2024.

# First Absence of DME (CST <325 µm) Achieved Faster by Patients Starting on Faricimab Vs Aflibercept[1]




Faricimab modified T&E regimen started at Week 100 for faricimab Q8W and aflibercept Q8W but not all patients received faricimab at Week 100. Summaries of time to first absence of DME are Kaplan–Meier estimates. Patients with absence of DME at baseline and patients with no data at baseline were excluded from the analysis. Afl, aflibercept; CST, central subfield thickness; DME, diabetic macular edema; EOS, end of study; Far, faricimab; QXW, every X weeks; T&E, treat-and-extend. 1. Data on File.

# Faricimab Was Well Tolerated Through Years 3 And 4 Of RHONE-X With The Nature Of AEs Consistent With The YOSEMITE/RHINE Parent Trials[1]

| | RHONE-X | | |
|---|---|---|---|
| **AEs Through Study End, Patients With ≥ 1 AE, n (%)[a]** | **Faricimab T&E (prior Q8W) n = 491** | **Faricimab T&E n = 500** | **Faricimab T&E (prior aflibercept) n = 473** |
| **Ocular AEs[b]** | 219 (44.6%) | 188 (37.6%) | 197 (41.6%) |
| **Serious ocular AEs[b]** | 31 (6.3%) | 15 (3.0%) | 26 (5.5%) |
| **Ocular AEs of special interest[c]** | 30 (6.1%) | 14 (2.8%) | 24 (5.1%) |
| **Intraocular inflammation events[d]** | 7 (1.4%) | 7 (1.4%) | 5 (1.1%) |
| Uveitis | 3 (0.6%) | 1 (0.2%) | 0 |
| Iritis | 2 (0.4%) | 4 (0.8%) | 1 (0.2%) |
| Iridocyclitis | 0 | 2 (0.4%) | 3 (0.6%) |
| Vitritis | 1 (0.2%) | 1 (0.2%) | 2 (0.4%) |
| Post-procedural inflammation | 1 (0.2%) | 0 | 0 |
| **Endophthalmitis events** | 2 (0.4%) | 0 | 1 (0.2%) |
| **Retinal vasculitis/retinal occlusive vasculitis events** | 0 | 0 | 0 |
| **Retinal vascular occlusion events (not associated with inflammation)** | | | |
| Retinal vein occlusion | 4 (0.8%) | 4 (0.8%) | 1 (0.2%) |
| Retinal artery occlusion | 0 | 1 (0.2%) | 2 (0.4%) |
| Retinal artery embolism | 0 | 0 | 0 |
| Arterial occlusive disease | 0 | 0 | 0 |
| **Serious non-ocular AEs** | 122 (24.8%) | 100 (20.0%) | 112 (23.7%) |
| **APTC events[e]** | 27 (5.5%) | 24 (4.8%) | 26 (5.5%) |

Safety data are presented only for the safety evaluation population from RHONE-X who are defined as patients who received at least one dose of faricimab in the RHONE-X long-term extension study. Includes AEs with onset from the first dose of study drug through study end. [a]Percentages are based on n values in the column headings; multiple occurrences of the same AE in an individual are counted only once. [b]Ocular AEs in the study eye only are presented. [c]Ocular AEs of special interest were defined as events associated with severe intraocular inflammation, events requiring surgical or medical intervention to prevent permanent loss of sight or events associated with BCVA loss of ≥30 letters for >1 hour. [d]Excluding endophthalmitis. [e]APTC events were adjudicated by an external independent committee; all other events were investigator reported. AE, adverse event; APTC, Antiplatelet Trialists' Collaboration; BCVA, best-corrected visual acuity; T&E, treat-and-extend; QXW, every X weeks. 1. Khanani AM *et al.* ASRS 2024.

# RHONE-X Demonstrated The Long-Term Safety And Efficacy Of Dual Ang-2/VEGF-A Inhibition With Faricimab In DME[1]

RHONE-X is the largest DME open-label extension study to date and had excellent patient retention (81.7%)

- BCVA and CST **improvements** in YOSEMITE/RHINE were **maintained** with ~80% of patients on ≥Q12W dosing at the end of study
- **Absence of DME** (CST <325 µm) was achieved in **over 90% of patients** by the end of the study
- First **absence of DME** was **achieved faster** by patients starting on **faricimab** vs aflibercept[2]
- Faricimab was **well tolerated** with a safety profile that was **consistent** with YOSEMITE/RHINE

Ang-2, angiopoietin-2 ; CST, central subfield thickness; DME, diabetic macular edema; Q12W, every 12 weeks; VEGF, vascular endothelial growth factor.
1. Khanani AM *et al.* ASRS 2024; 2. Data on File.

# Key Takeaways

**Objective**

We have demonstrated why **faricimab** could be an important first line treatment to **optimise** outcomes


**How is this achieved?**

**Dual pathway**, **Drying**, and **Durability**

**How do we know this?**

**Clinical trial data** are reflected in the **real-world**

# Key Takeaways

**Objective**

We have demonstrated why **faricimab** could be an important first line treatment to **optimise** outcomes


**DURABILITY**

**How do we know this?**

**Clinical trial data** are reflected in the **real-world**

# Thank You For Listening

If you wish to download a copy of these slides, please scan the QR code above.