Nuovi approcci di trattamento per la gestione dell'edema maculare diabetico

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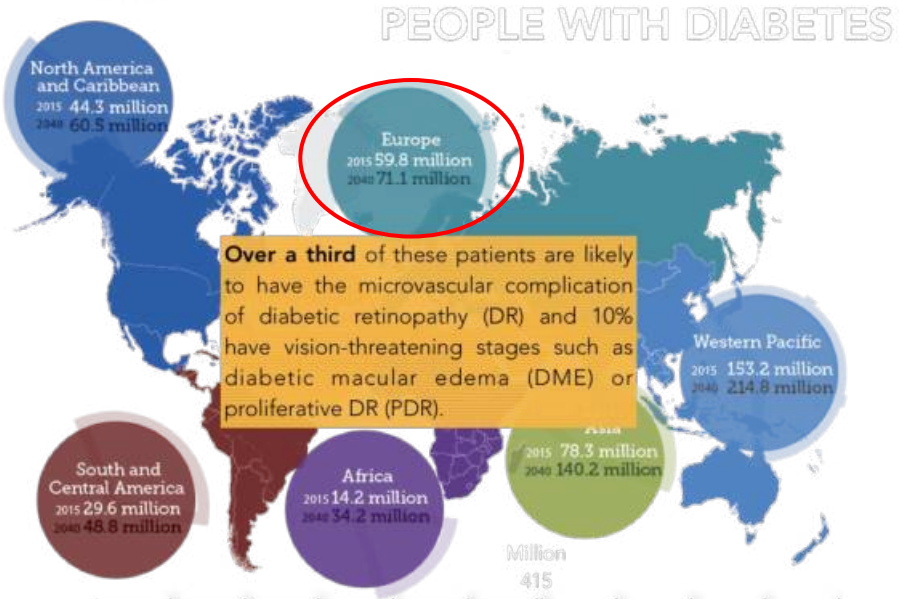
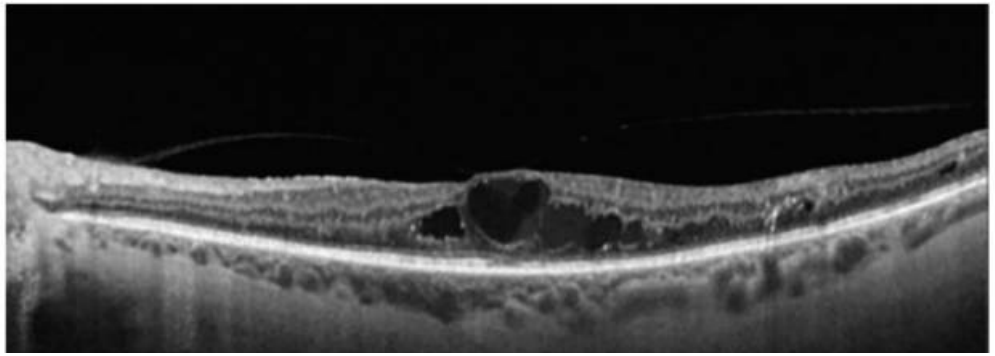
Diabetic Macular Edema

- Diabetic retinopathy (DR) is a leading cause of vision loss among adults, affecting millions of people worldwide.[1]
- On a global scale, the prevalence rate is estimated to be 34.6%, encompassing approximately 93 million people. [2]
- Diabetic macular edema (DME) stands as the leading cause of vision loss among individuals with diabetes
- The disruption of the blood-retinal barrier (BRB) in DME can lead to the buildup of plasma proteins, lipids, and extracellular fluid within the macula

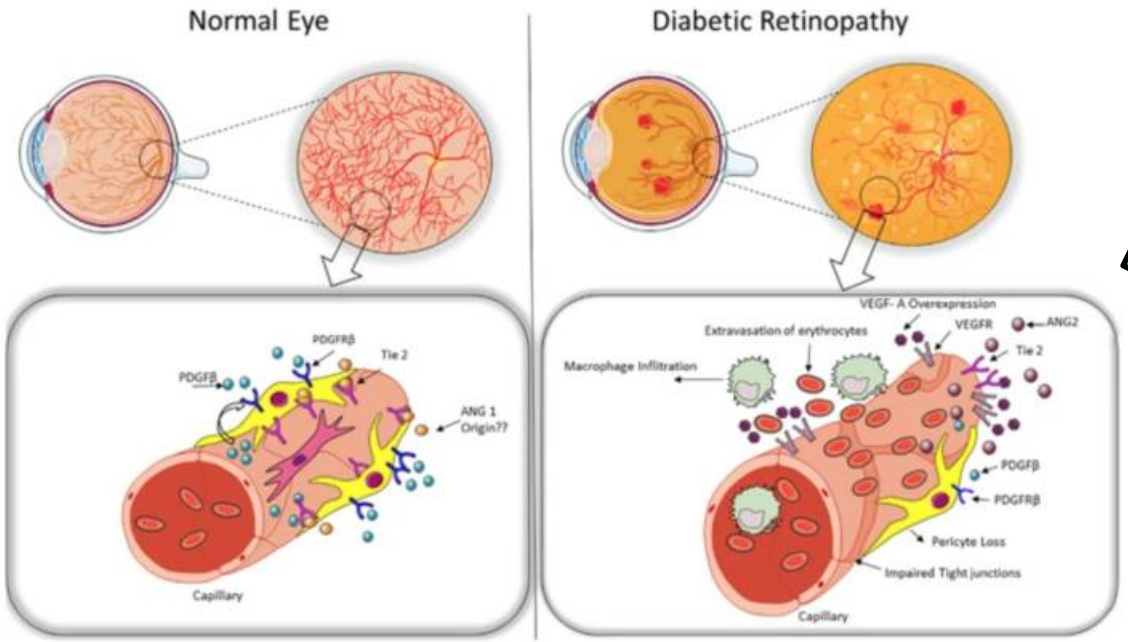
1 in 10 diabetic patients suffers from DME

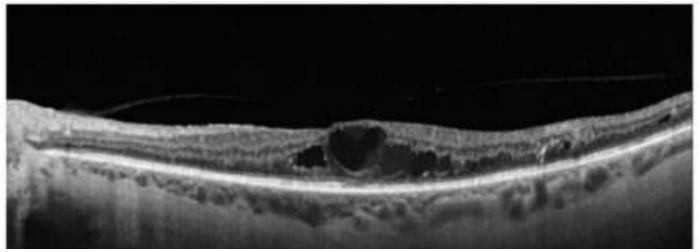


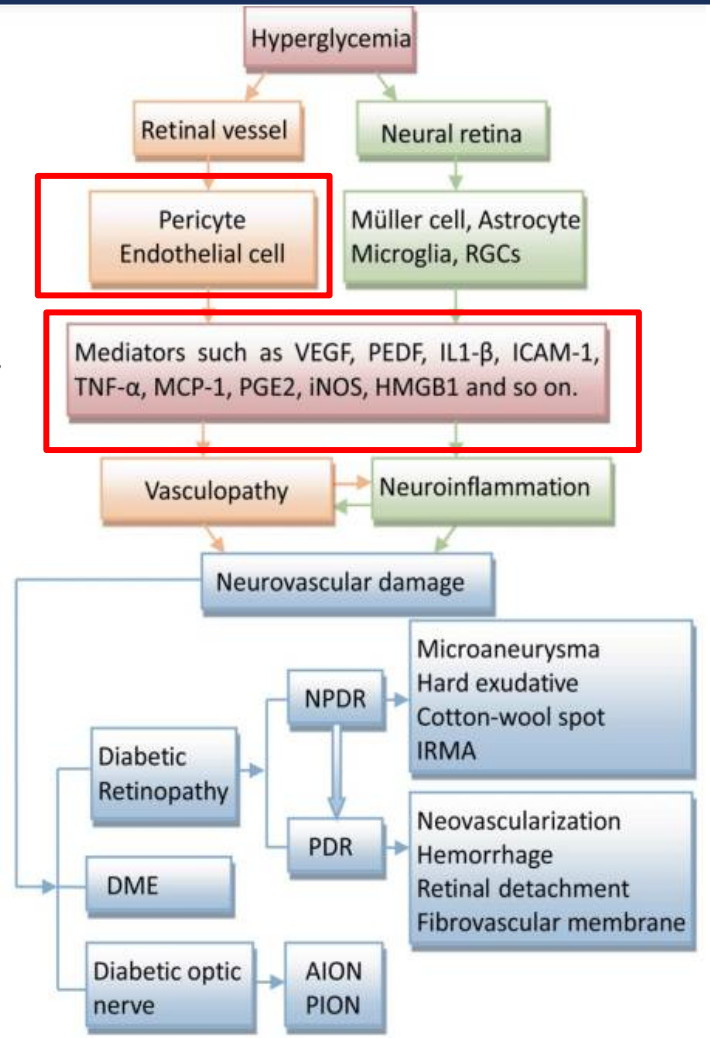


1. Yau, J. W. et al. Meta-Analysis for Eye Disease (META-EYE) Study Group. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012, 35, 556–64.
2. Lin KY et al. Update in the epidemiology, risk factors, screening, and treatment of diabetic retinopathy. J Diabetes Investig. 2021;12(8):1322-1325.

Biochemical Pathways





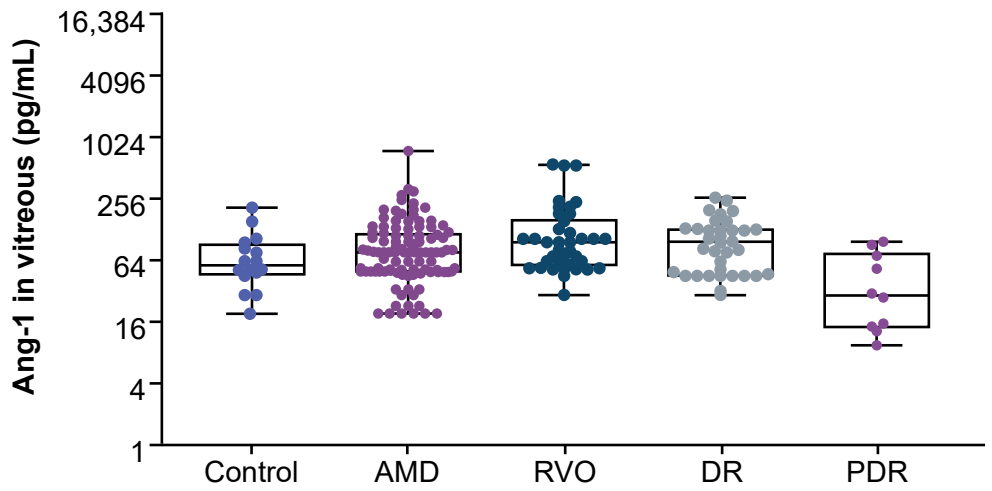


Chan et al. Optimizing treatment for diabetic macular edema during cataract surgery. 2023

Ang-2 levels are upregulated in several retinal diseases, supporting a role for the Ang-2/Tie2 pathway in pathological conditions

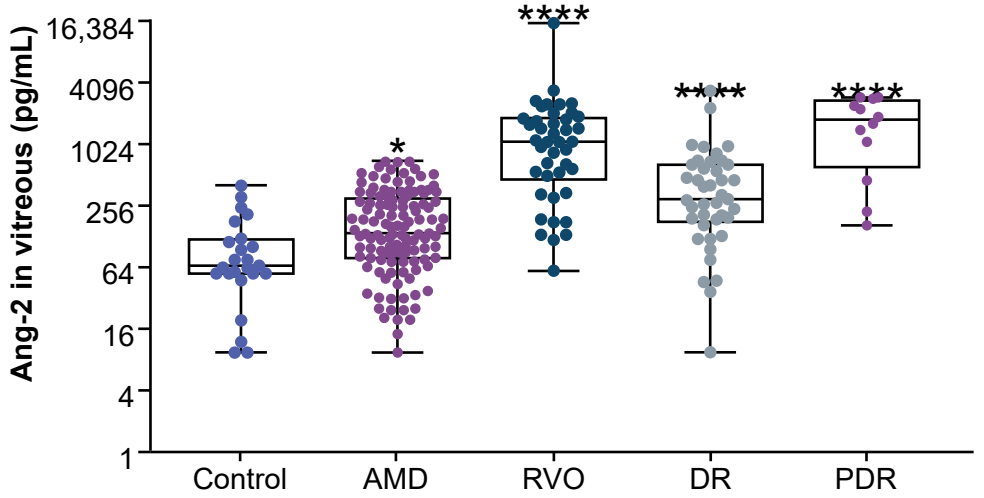
Human vitreous samples

Ang-1 levels



Ang-1 is constitutively expressed to maintain **vasculature homeostasis**

Ang-2 levels

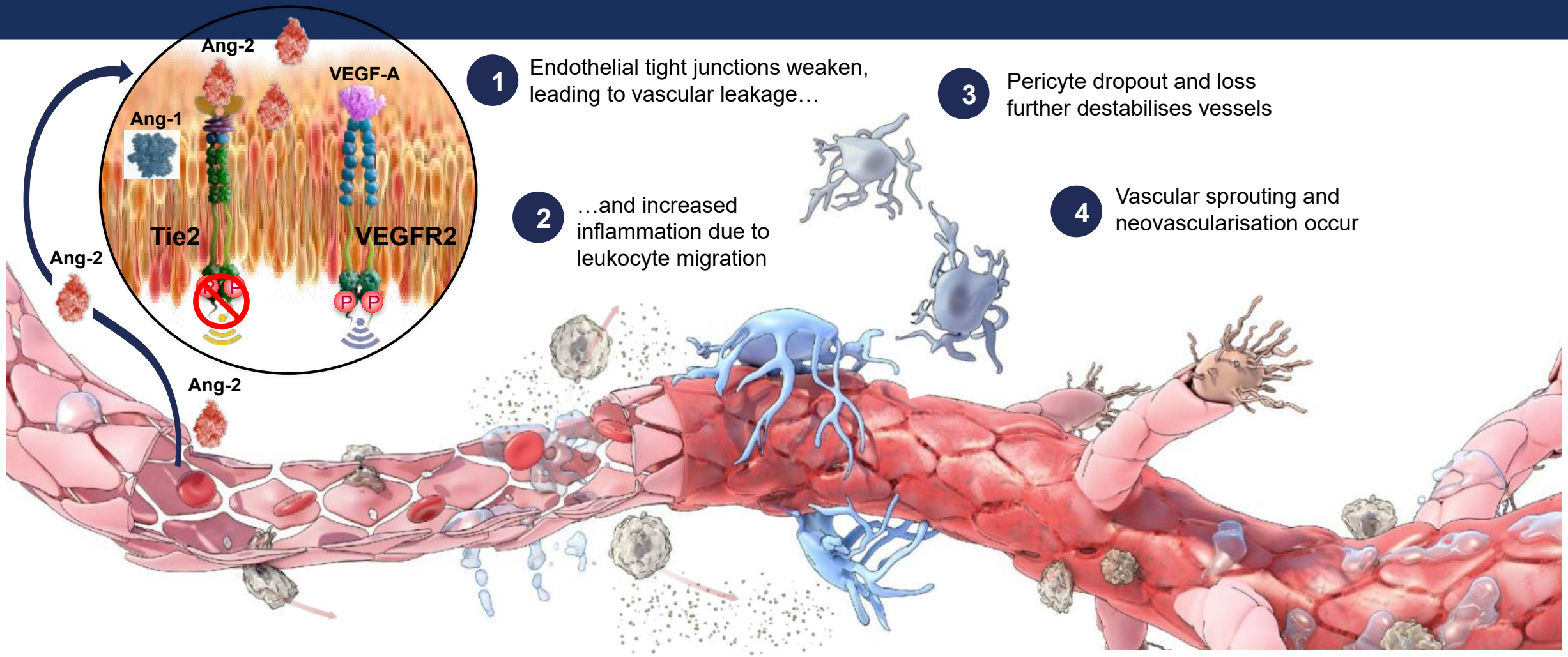


Ang-2 levels are upregulated under **pathological conditions**

*p<0.05; ****p<0.0001. A nonparametric Kruskal–Wallis analysis followed by Dunn's method for multiple comparisons was used to show significant differences of the groups to control, which are indicated by asterisks. Ang-1 levels did not differ significantly, but Ang-2 levels were significantly different. AMD, age-related macular degeneration; Ang, angiopoietin; DR, diabetic retinopathy; RVO, retinal vein occlusion; PDR, proliferative diabetic retinopathy; Tie2, tyrosine kinase with immunoglobulin-like domains 2

Regula JT, et al. EMBO Mol Med. 2016;8:1265–88; Regula JT, et al. EMBO Mol Med. 2019;11:e10666

Pathologic tissues: Elevated levels of Ang-2 and VEGF-A lead to vascular instability[1–5]



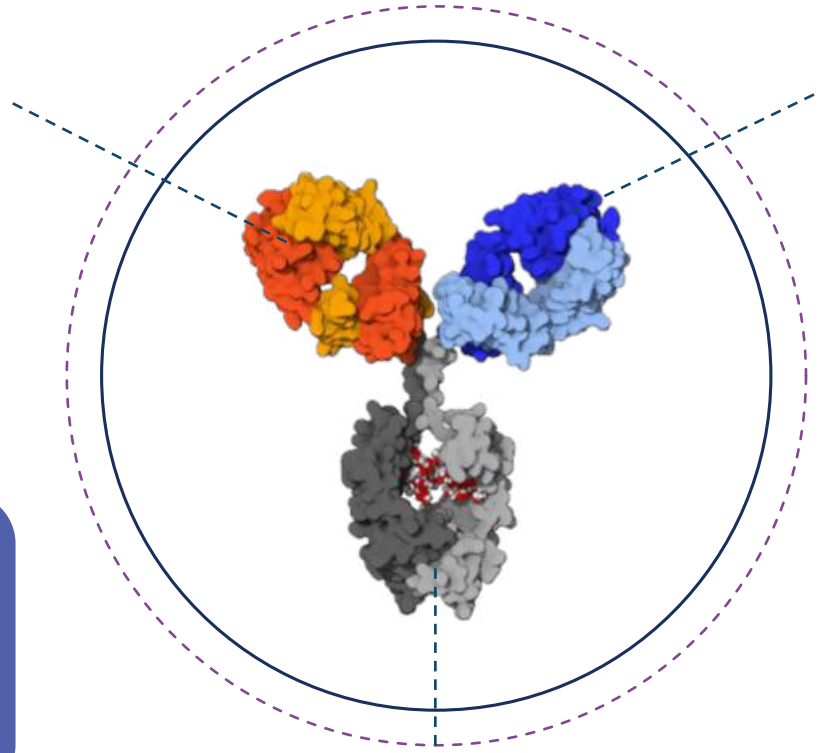
Adapted from Angiopoietin_Infographic.pdf, https://www.scienceofang2.org/, Copyright 2020. The Angiogenesis Foundation

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

1. Csaky KG, et al. Dual inhibition of Ang-2 and VEGF-A with faricimab: Advances in understanding and treatment of retinal diseases. Presented at Angiogenesis Congress 2021; 2. Fiedler U, Augustin HG. Trends Immunol. 2006;27:552–558; 3. Saharinen P, et al. Nat Rev Drug Discov. 2017;16:635–661; 4. Clapp C, et al. Physiol Rev. 2009;89:1177–1215; 5. Bolinger MT, et al. Int J Mol Sci. 2016;17:1498

Faricimab: 1 Molecule With 2 Disease Pathways via Ang-2 and VEGF-A to Improve Vascular Stability for Durable Efficacy

Anti–Ang-2 Fab
Stabilizes vessels
Reduces vascular leakage
Reduces inflammation



Anti–VEGF-A Fab
Reduces vascular leakage
Inhibits neovascularization

Multifactorial retinal and choroidal vascular diseases may require neutralization of more than just the VEGF pathway

Modified Fc
Reduces systemic exposure
Reduces inflammatory potential

Dual inhibition of Ang-2 and VEGF-A withx faricimab may result in stabilized vessels and reduced neovascularization, leading to **durable efficacy** when treating retinal diseases

CrossMAb molecule representative of faricimab. Regula JT et al. *EMBO Mol Med*. 2016;8(11):1265-1288, with erratum in Regula JT et al. *EMBO Mol Med*. 2019;11(5):e10666.
Ang-2, angiopoietin-2; Fab, fragment antigen binding; Fc, fragment crystallizable; VEGF, vascular endothelial growth factor; VEGF-A, vascular endothelial growth factor-A.
Medicinale sottoposto a monitoraggio addizionale. Ciò permetterà la rapida identificazione di nuove informazioni sulla sicurezza . Agli operatori sanitari è richiesto di segnalare qualsiasi reazione avversa sospetta.
Vedere paragrafo 4.8 dell'RCP per informazioni sulle modalità di segnalazione delle reazioni avverse

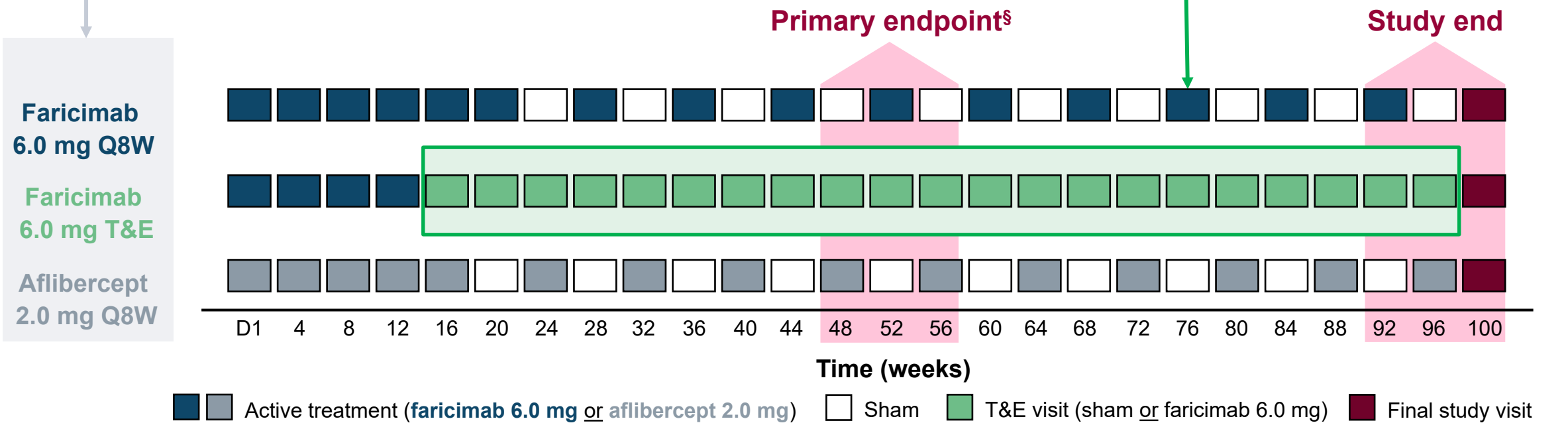
YOSEMITE & RHINE trial design: Faricimab DME trials use disease criteria reflective of clinical practice

Treatment-naïve or **previously treated patients*** (1 eye per patient);
YOSEMITE= 940, RHINE= 951

- Centre-involving DME (**CST ≥325 µm**)†
- **BCVA 25–73 ETDRS letters** (Snellen ~20/320–20/40)‡

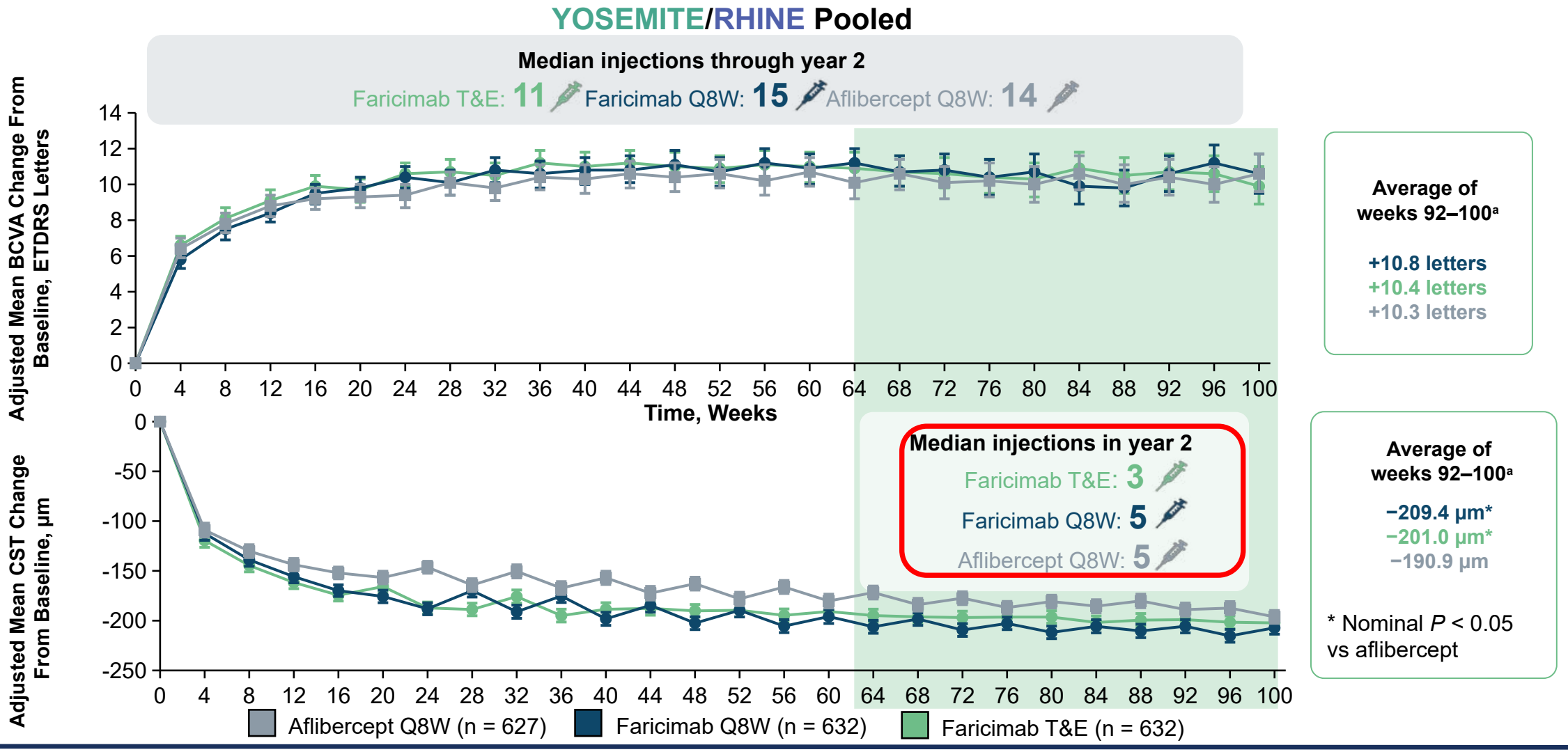
Personalised T&E–based dosing regimen

- Dosing **extended** (by 4 weeks, max Q16W) based on stable **CST AND BCVA**
- Dosing **reduced** (by 4 or 8 weeks, min Q4W) based on worsening of **CST** ± worsening of BCVA
- Dosing **maintained** if extension or reduction criteria not met



YOSEMITE clinical trial (NCT03622580); RHINE clinical trial (NCT03622593). *Previously anti-VEGF–treated eyes (treated ≥3 months before day 1) were limited to 25% of the total enrolment; †CST was measured as the distance from the ILM to Bruch's membrane; ‡BCVA was measured using the ETDRS VA chart at a starting distance of 4 m; §primary efficacy endpoint: adjusted mean BCVA change from baseline at 1 year, averaged over Weeks 48, 52 and 56; Presented by Khanani AM at Angiogenesis February 10–11, 2023

Robust Vision Gains and Greater CST reduction With Faricimab at Year 1 Were Maintained Through Year 2



Average of weeks 92–100[a]

+10.8 letters
+10.4 letters
+10.3 letters

Average of weeks 92–100[a]

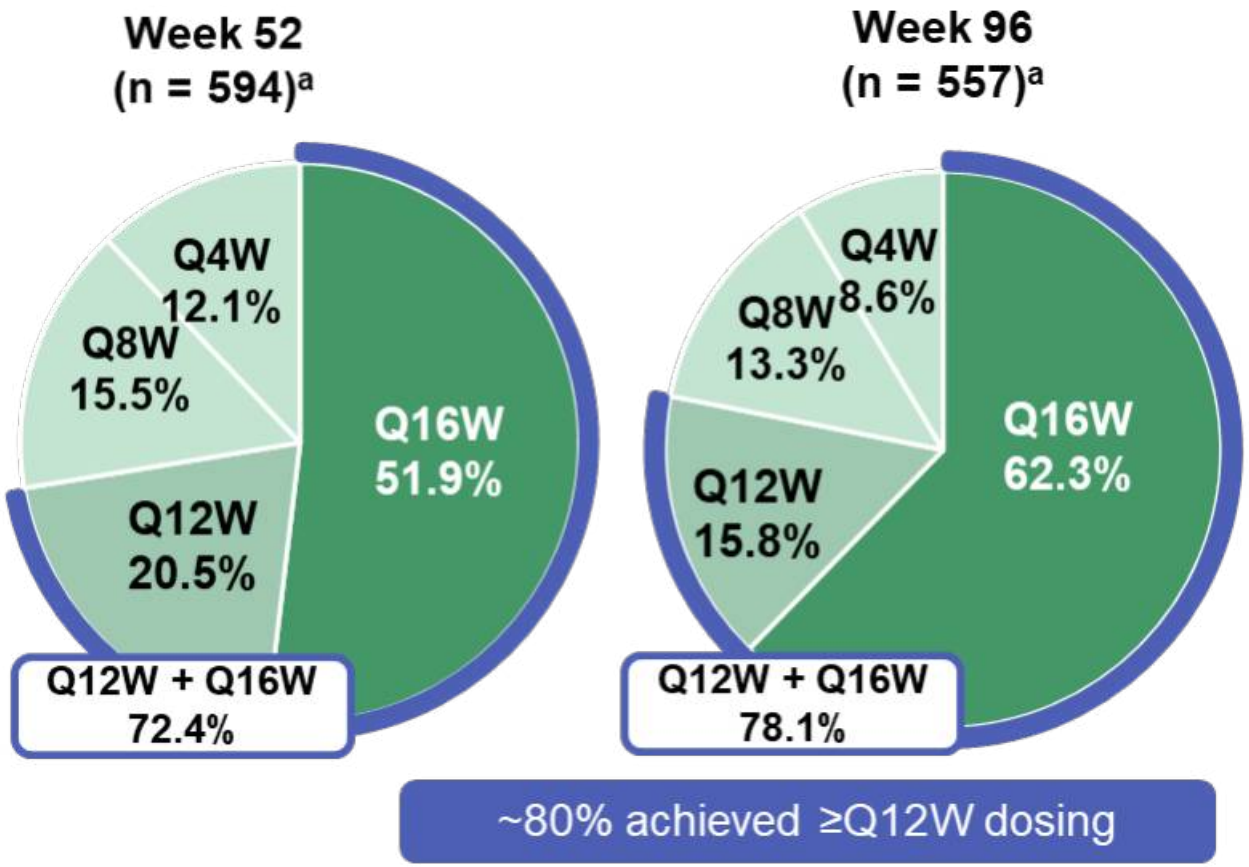
−209.4 µm*
−201.0 µm*
−190.9 µm

* Nominal $P < 0.05$ vs aflibercept

[a] Adjusted mean change from baseline at 2 years, 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 BCVA (continuous) as applicable, 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; ETDRS, Early Treatment Diabetic Retinopathy Study; Q8W, every 8 weeks; T&E, treat-and-extend; VEGF, vascular endothelial growth factor. Presented by Khanani AM at Angiogenesis February 10–11, 2023

In Year 2, faricimab up to Q16W achieved durable vision gains with fewer injections vs aflibercept in patients with DME

YOSEMITE/RHINE pooled



In Year 2†
Median number of injections

Faricimab T&E:
3

Faricimab Q8W:
5

Aflibercept Q8W:
5

*Proportion of patients in the pooled faricimab T&E arms on Q4W, Q8W, Q12W or Q16W dosing at Week 96, among those who had not discontinued the study at the Week 96 visit; results are presented for the pooled YOSEMITE/RHINE safety-evaluable population (faricimab Q8W, n=630; faricimab T&E, n=632; aflibercept Q8W, n=625); †Weeks 60–96. Presented by Khanani AM at Angiogenesis February 10–11, 2023

Case report 1

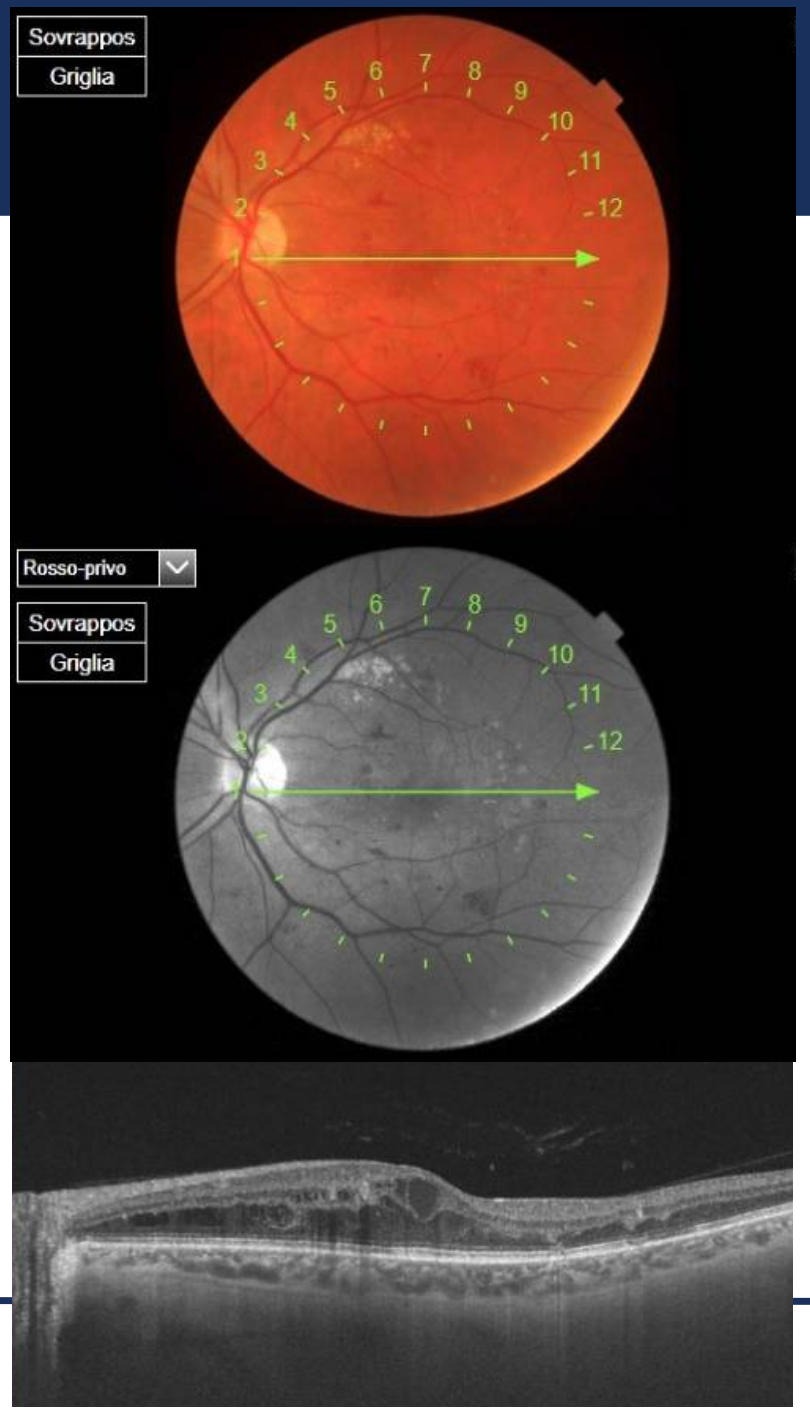
Patient history

Age: 45

Sex: Female

Diabetes duration: 5 years

Diabetic macular edema OU



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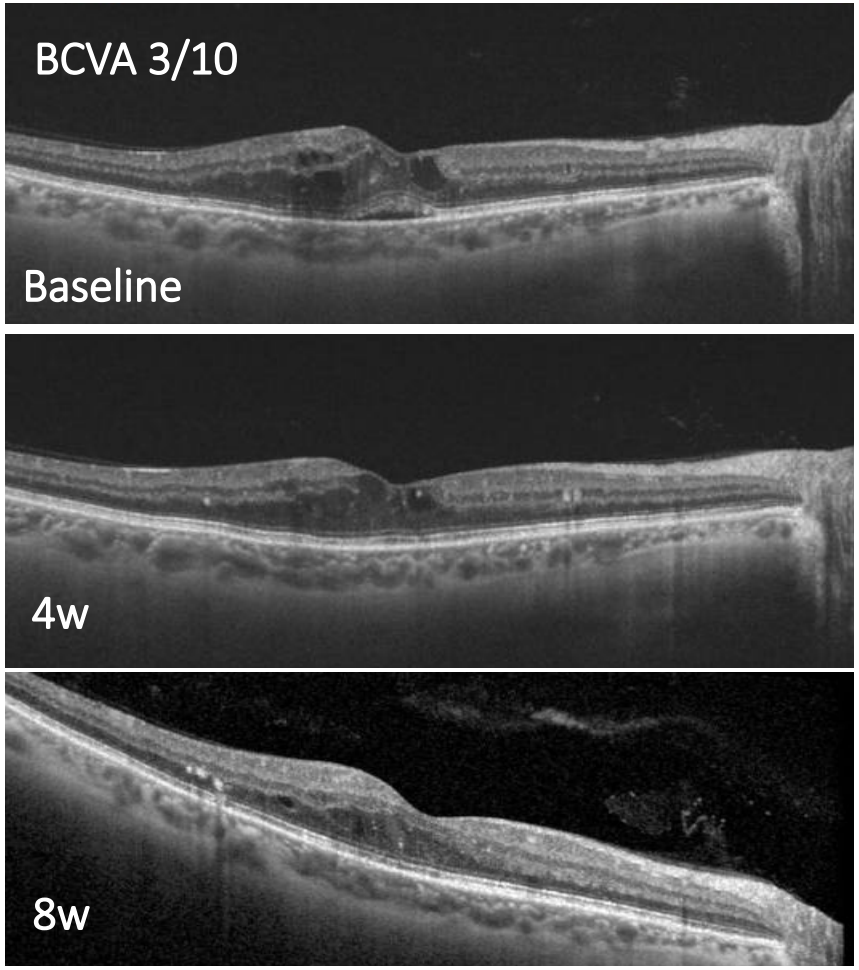
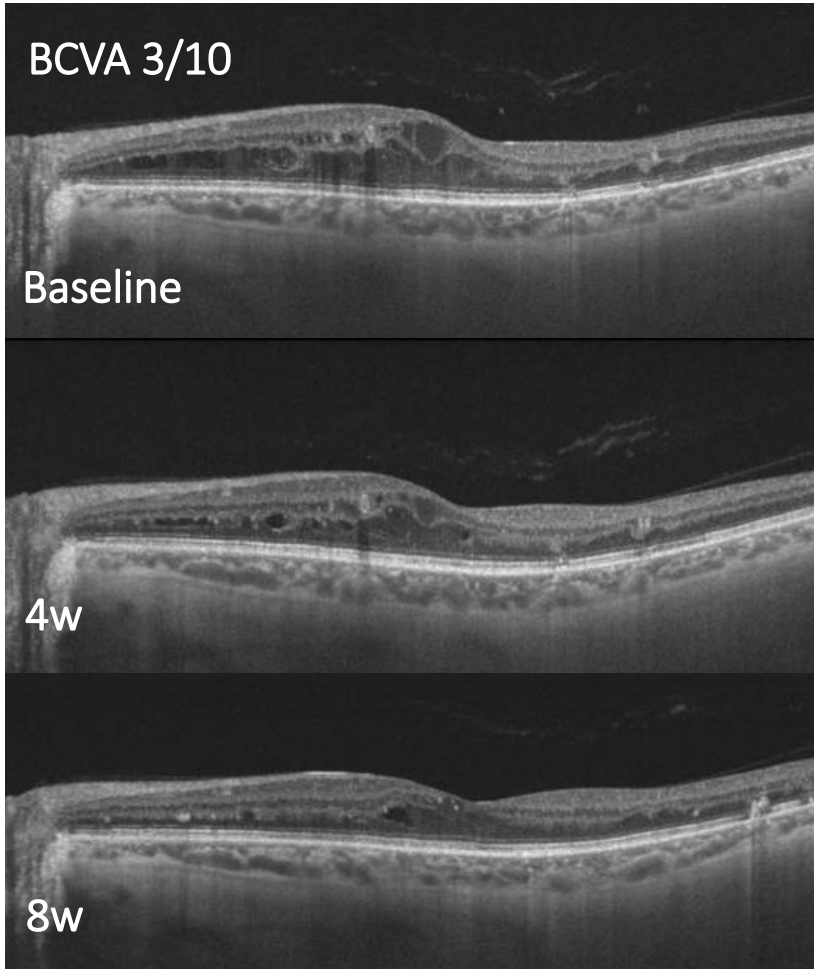
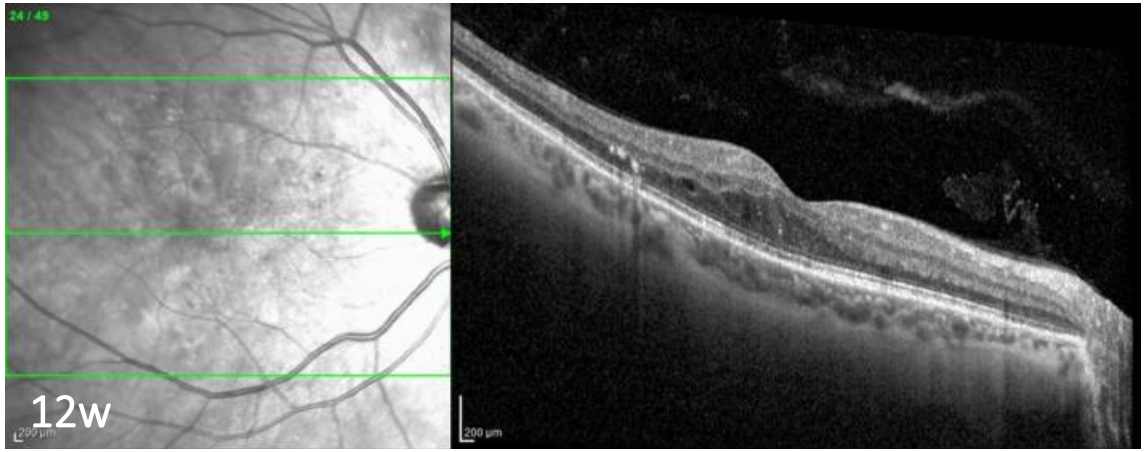
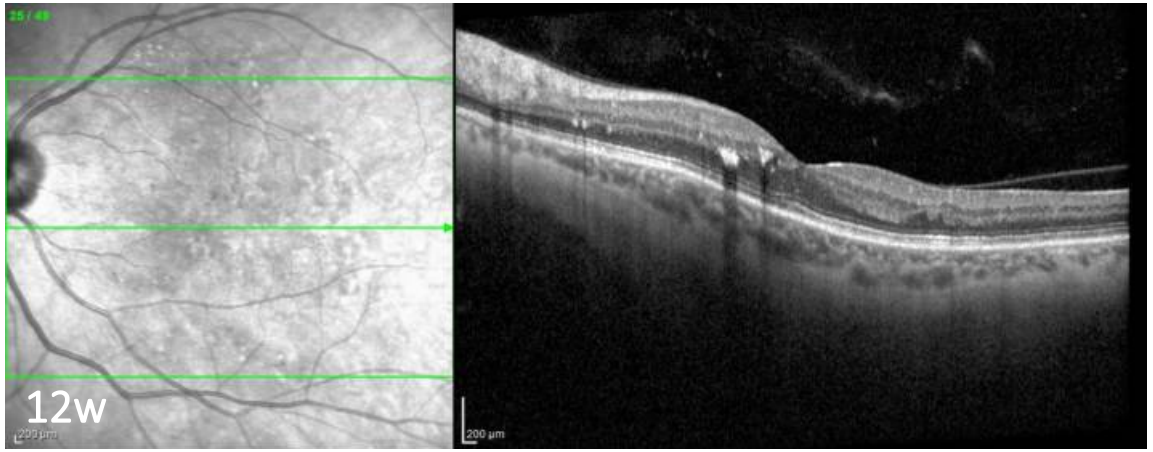
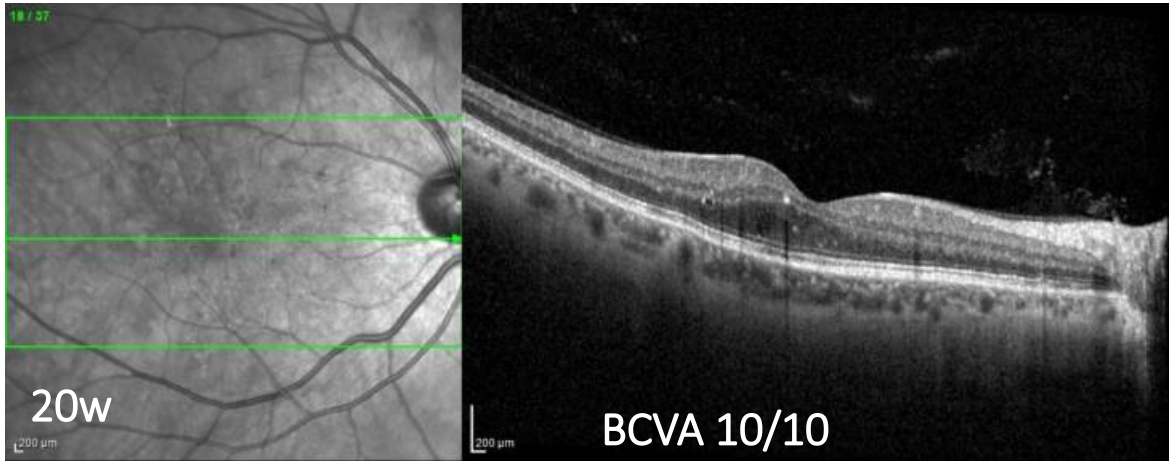


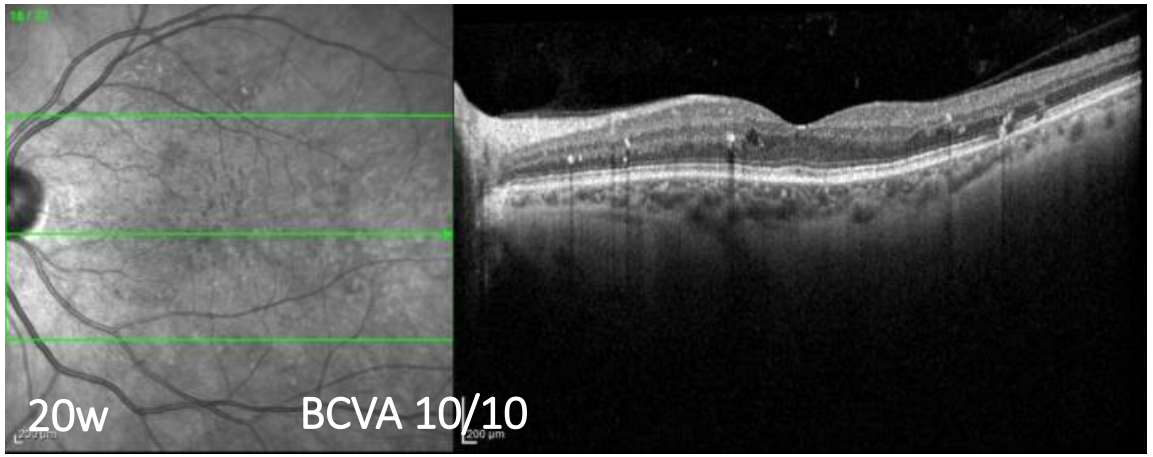


Case report 1





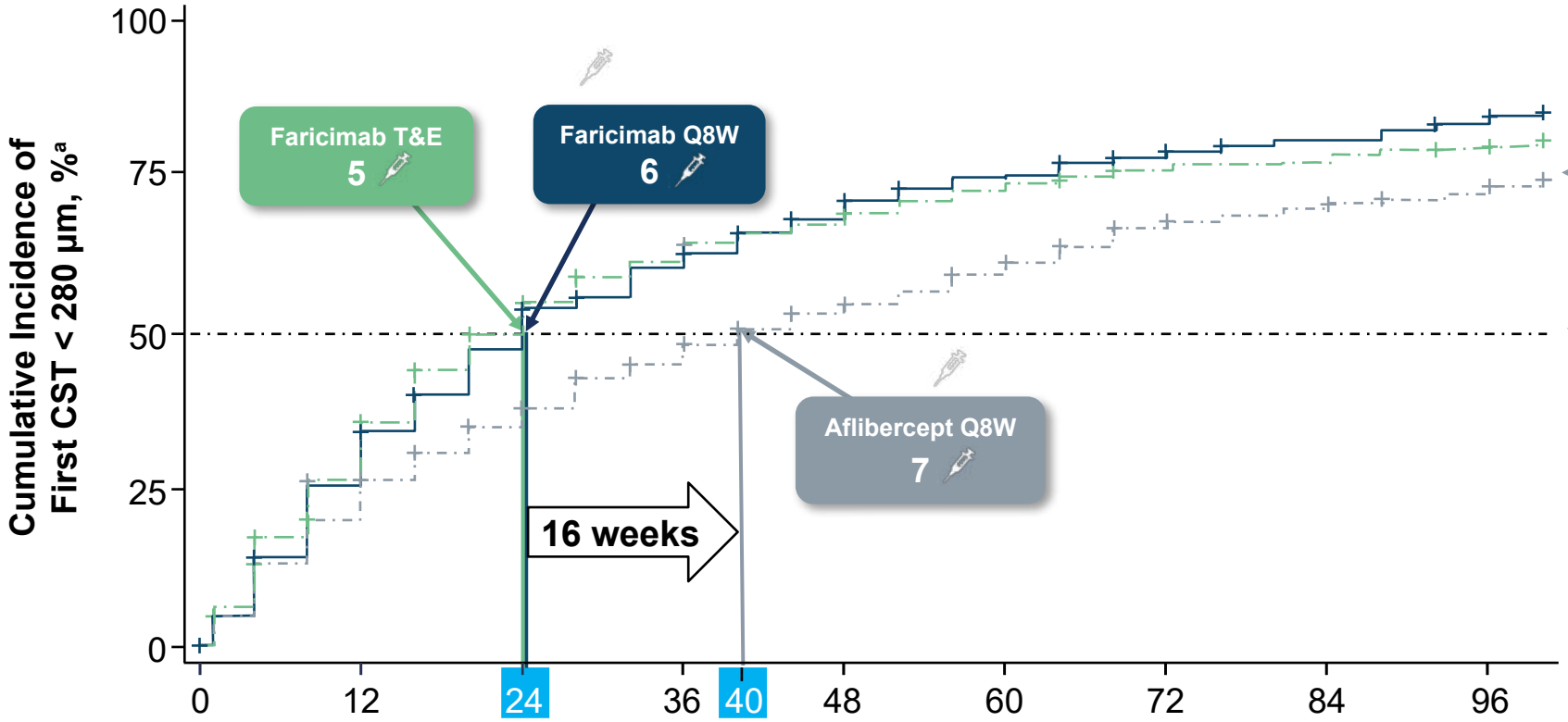




Median Time to First CST < 280 µm: Achieved With Faricimab 16 Weeks Faster and With Fewer Injections vs Aflibercept

ITT population
Patients with CST ≥ 280 µm at baseline

YOSEMITE/RHINE Pooled: Post Hoc Analysis



75th percentile was not reached for aflibercept

50th percentile was reached 16 weeks earlier with faricimab vs aflibercept

\+ Censored

Median number of injections[b]

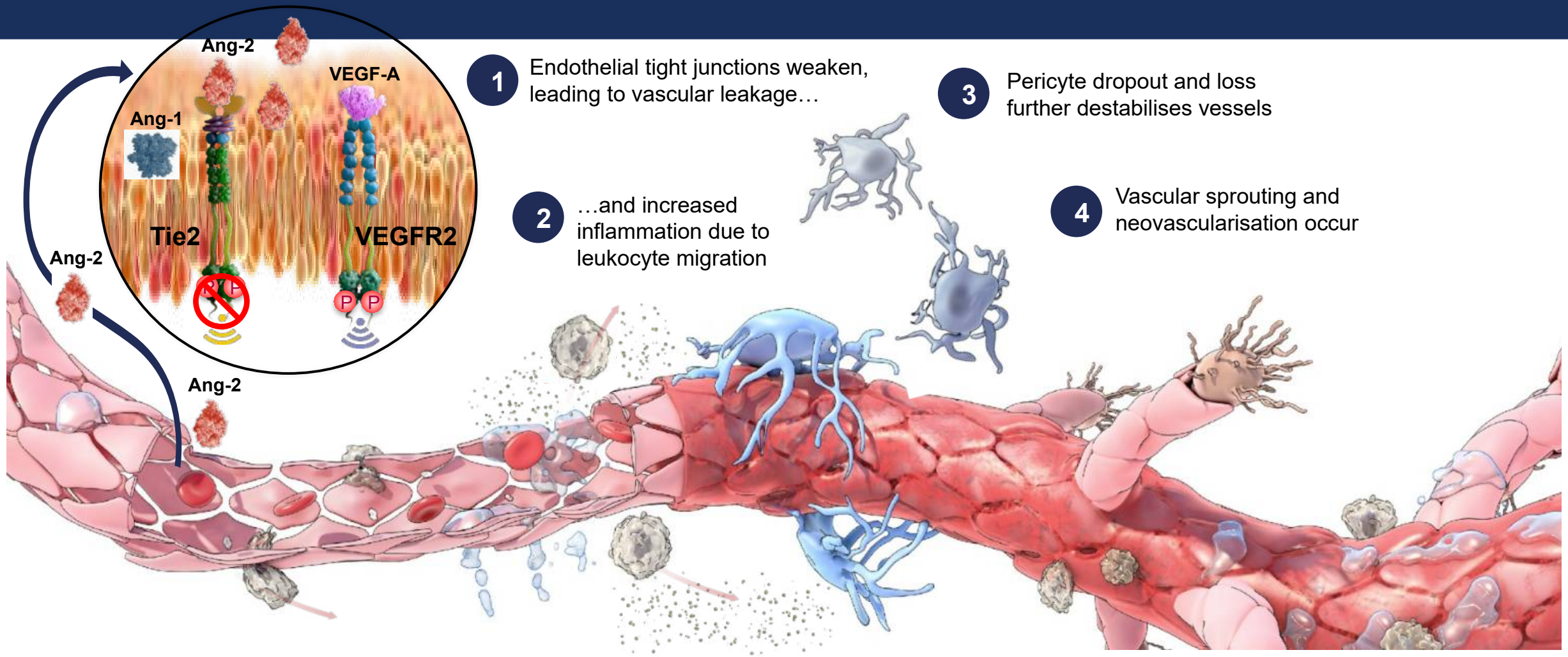
Patients at risk									
Aflibercept Q8W	617	485	388	320	270	232	181	164	141
Faricimab Q8W	625	460	322	239	185	145	123	107	88
Faricimab T&E	627	458	306	234	195	161	140	130	113

HR (95% CI)[c]: 1.47 (1.28, 1.68), *P* < 0.0001

HR (95% CI)[c]: 1.41 (1.23, 1.62), *P* < 0.0001

Summaries of time to CST < 280 µm are Kaplan-Meier estimates, with the time variable defined as the target visit week. Patients with CST < 280 µm 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 (US and Canada, Asia and the rest of the world) and study (YOSEMITE vs RHINE). [a] CST < 280 µm was measured as the distance from the ILM to Bruch's membrane. [b] The number of injections includes any active drug administered (faricimab or aflibercept), including medication errors. [c] Results from stratified analyses are presented for HR and log-rank test vs aflibercept. An HR > 1 favours faricimab over aflibercept. BCVA, best-corrected visual acuity; CI, confidence interval; CST, central subfield thickness; HR, hazard ratio; ILM, internal limiting membrane; ITT, intent to treat; Q8W, every 8 weeks; T&E, treat-and-extend; VEGF, vascular endothelial growth factor. Presented by Lanzetta P at Euretina 2023.

Pathologic tissues: Elevated levels of Ang-2 and VEGF-A lead to vascular instability[1–5]



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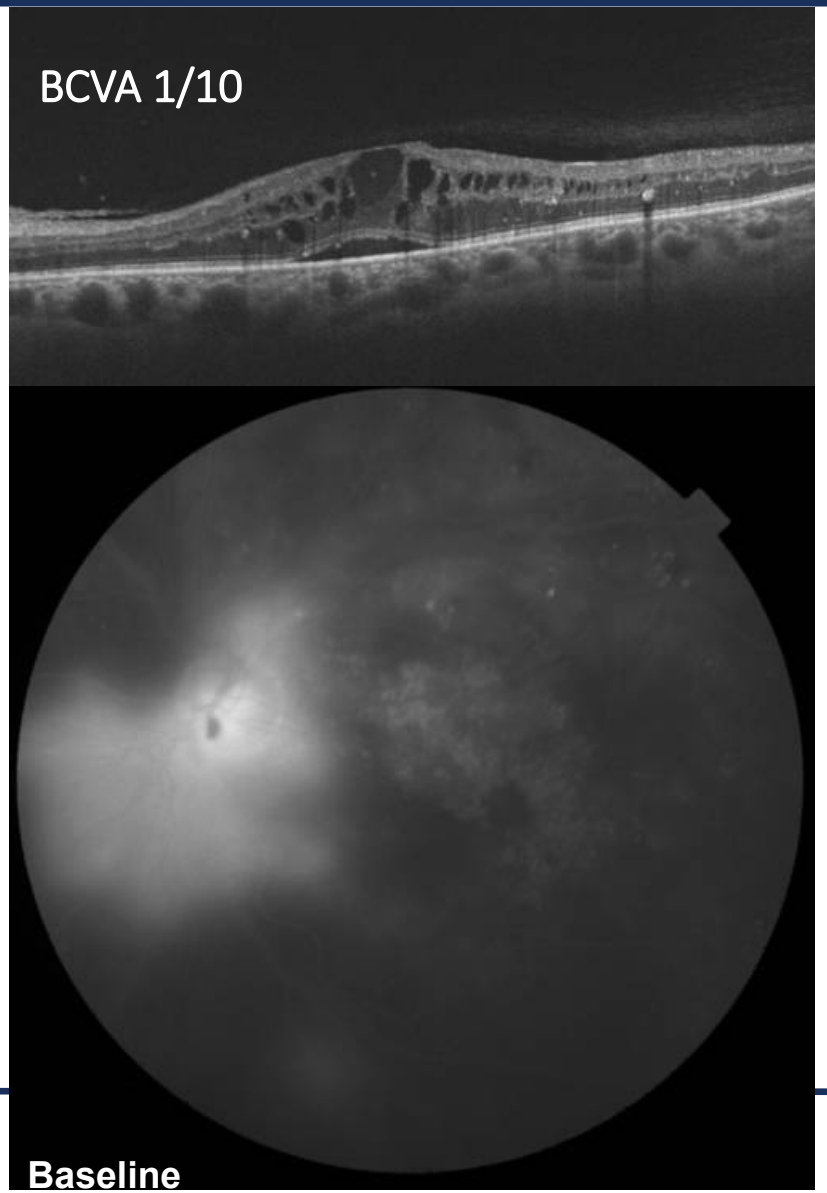
Ang, angiopoietin; Tie2, tyrosine kinase with immunoglobulin-like domains; VEGF-A, vascular endothelial growth factor-A; VEGFR2, vascular endothelial growth factor receptor 2

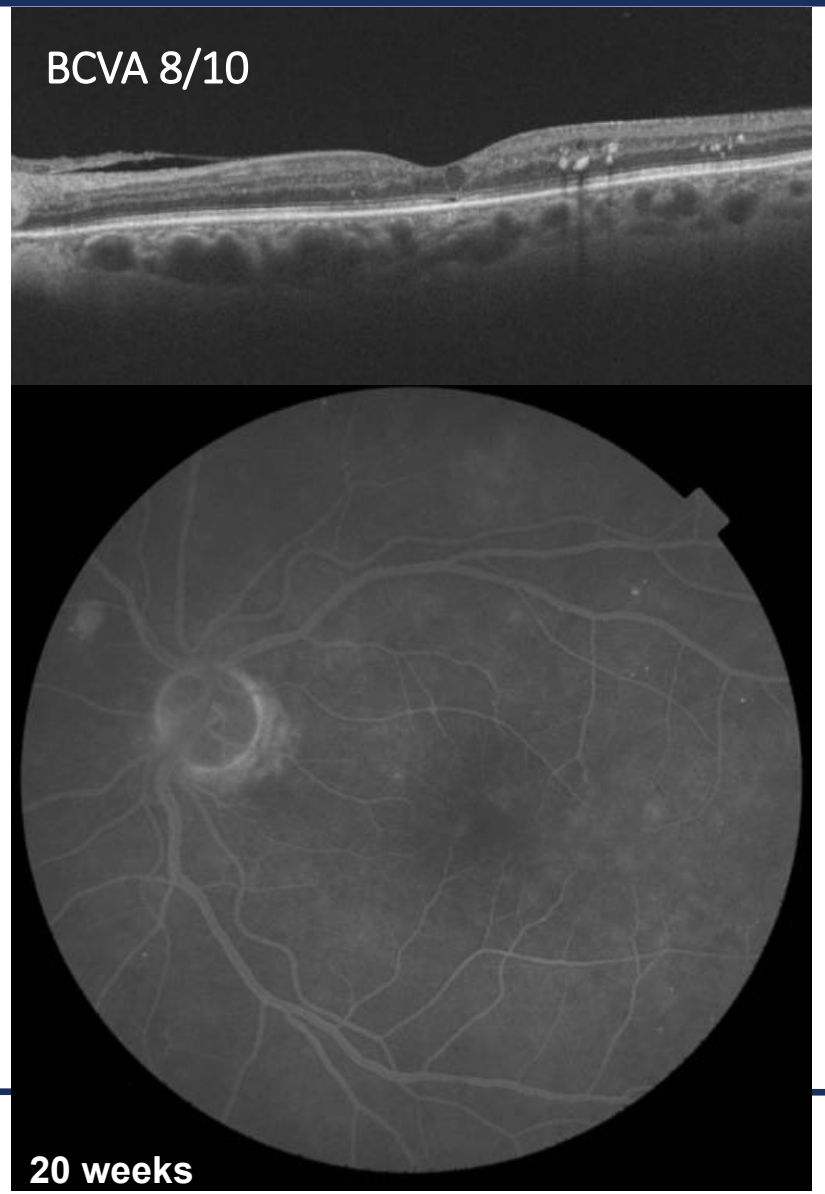
1. Csaky KG, et al. Dual inhibition of Ang-2 and VEGF-A with faricimab: Advances in understanding and treatment of retinal diseases. Presented at Angiogenesis Congress 2021; 2. Fiedler U, Augustin HG. Trends Immunol. 2006;27:552–558; 3. Saharinen P, et al. Nat Rev Drug Discov. 2017;16:635–661; 4. Clapp C, et al. Physiol Rev. 2009;89:1177–1215; 5. Bolinger MT, et al. Int J Mol Sci. 2016;17:1498

Case Report 2

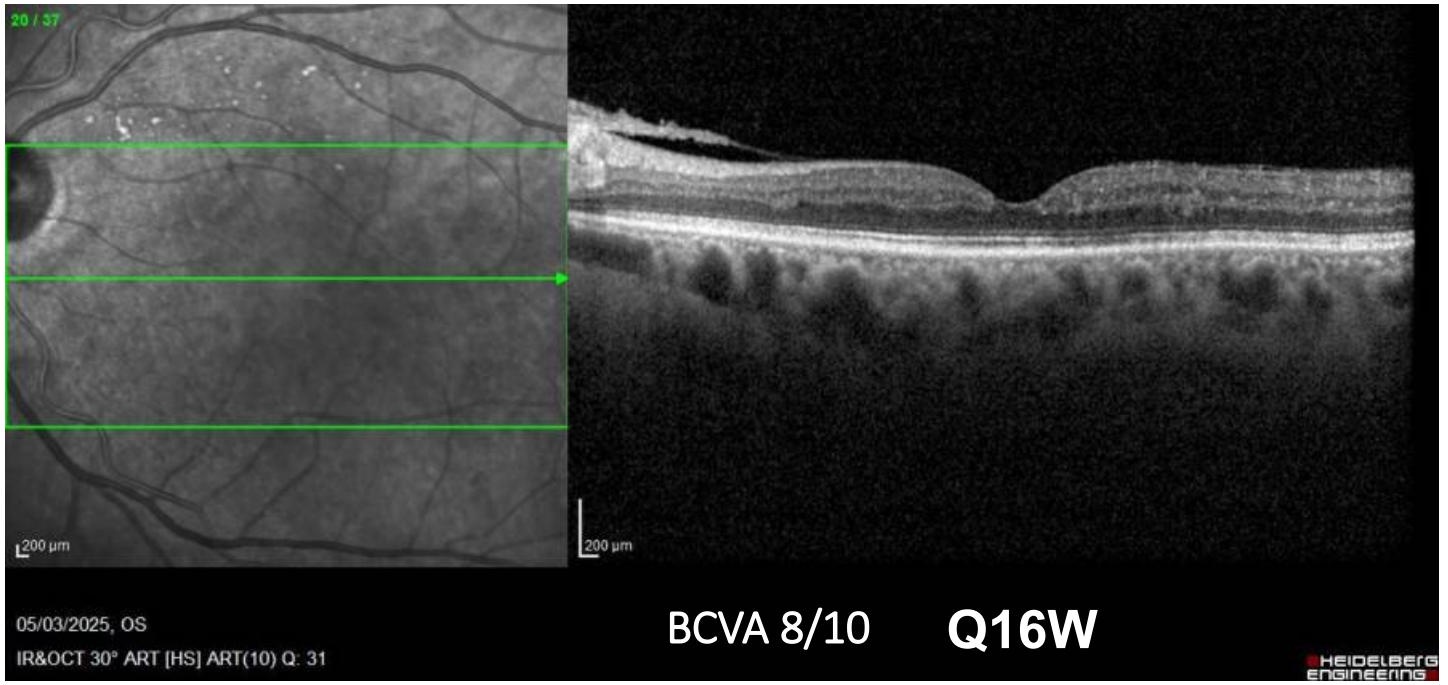
Patient history

Age: 51
Sex: Male
Diabetes duration: 7 years
Diabetic macular edema
Proliferative diabetic retinopathy





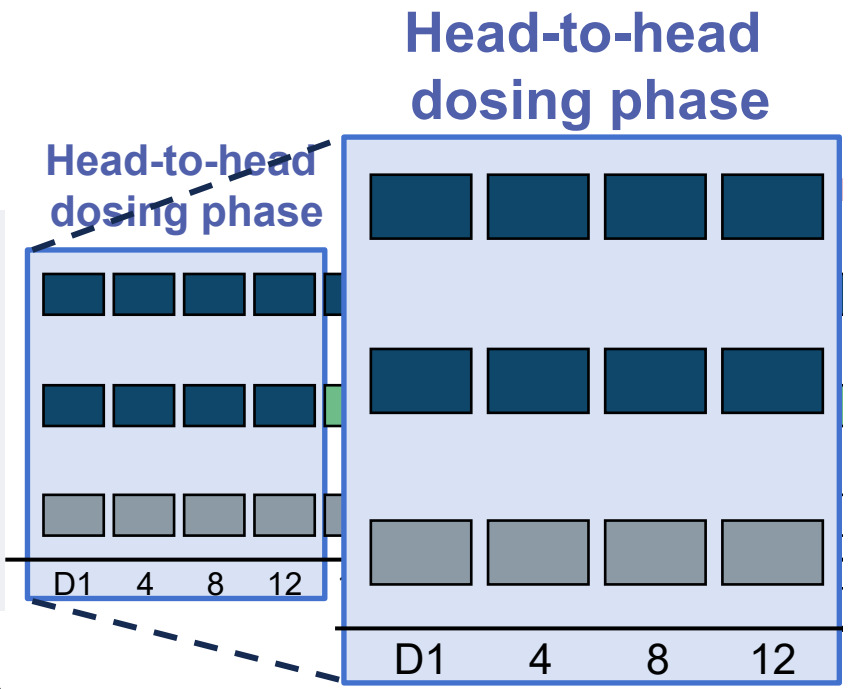
Case Report 2



Macular Leakage Was Evaluated During the Matched Head-to-Head Dosing Phase of YOSEMITE/RHINE

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

Faricimab 6.0 mg Q8W
Faricimab 6.0 mg T&E
Aflibercept 2.0 mg Q8W



Active treatment (**faricimab 6.0 mg** or **aflibercept 2.0 mg**)

Pre-specified Macular Leakage Area Assessments

- **Masked** readers from the Wisconsin Reading Centre
- Area within **ETDRS grid** on **FA images**

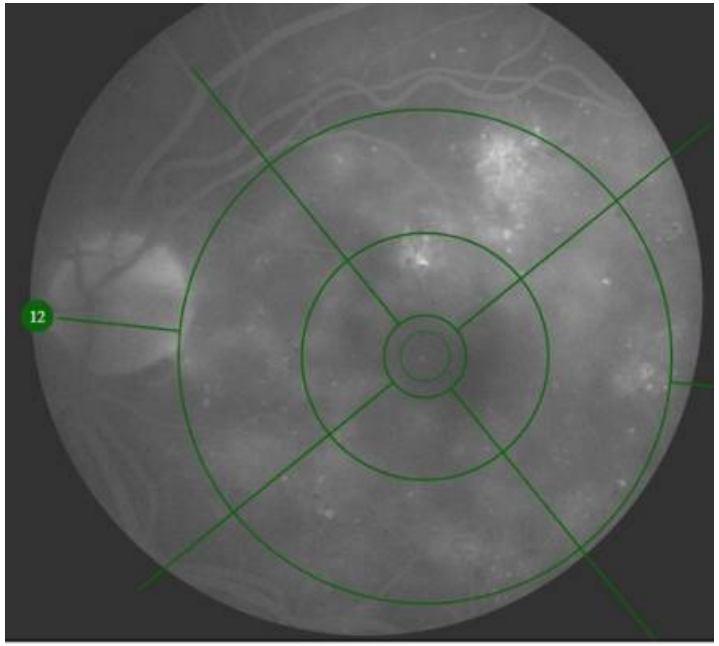


Image courtesy of Wisconsin Reading Centre.

Sham
T&E visit (sham or faricimab 6.0 mg)
Final study visit

YOSEMITE (NCT03622580); RHINE (NCT03622593). [a] Previously anti-VEGF–treated eyes (treated ≥ 3 months before day 1) were limited to 25% of the total enrolment. [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. d Primary efficacy endpoint: adjusted mean BCVA change from baseline at 1 year, averaged over weeks 48, 52 and 56. BCVA, best-corrected visual acuity; CST, central subfield thickness; D, day; DME, diabetic macular edema; ETDRS, Early Treatment Diabetic Retinopathy Study; FA, fluorescein angiography; ILM, internal limiting membrane; Q8W, every 8 weeks; T&E, treat-and-extend; VEGF, vascular endothelial growth factor. Presented by Tan CS at APAO February 22-25, 2023.

Reduced Macular Leakage Area With Faricimab vs Aflibercept in the Head-to-Head Dosing Phase

YOSEMITE/RHINE Pooled: Post Hoc Analysis

Median Baseline Macular Leakage Area

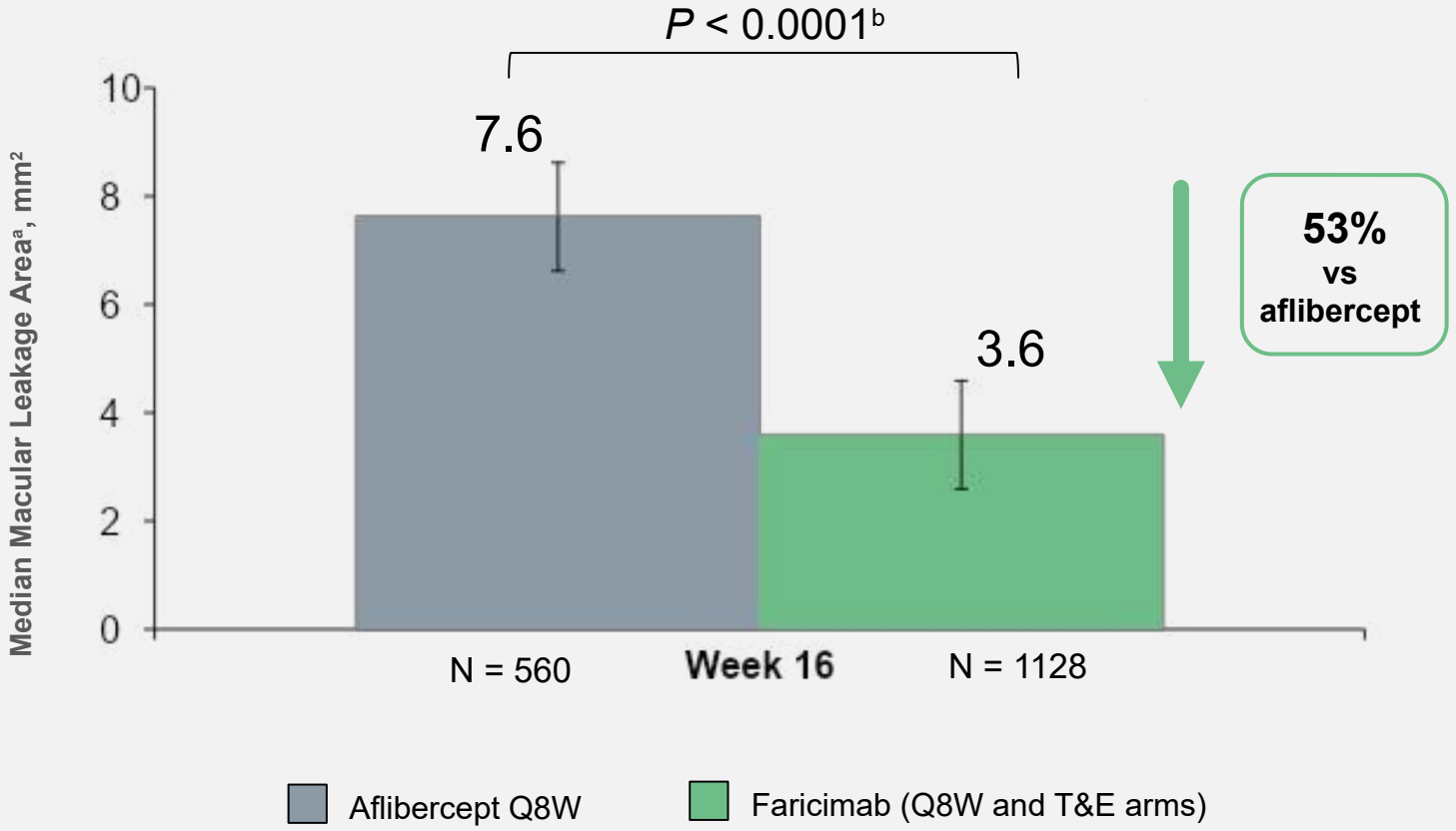
Aflibercept Q8W
(N = 593)

25.6 mm²

Faricimab (Q8W and T&E arms)
(N = 1216)

24.6 mm²

P = 0.3331[b]

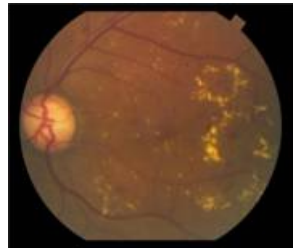


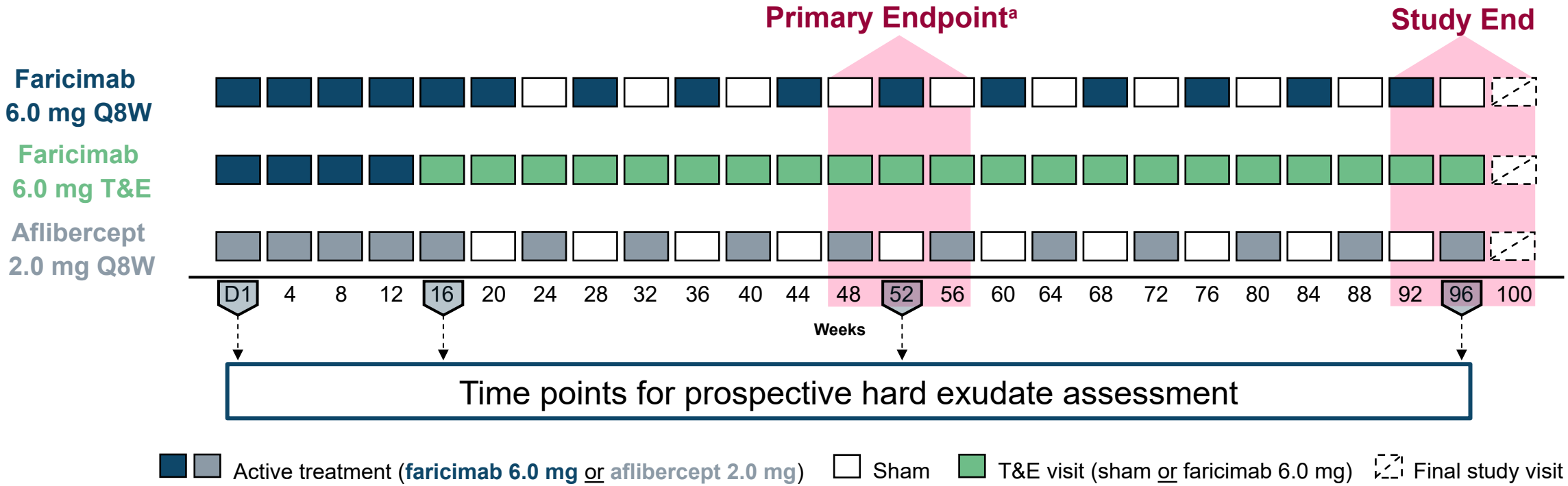
Population: patients with available macular leakage data at baseline or week 16 according to the timepoint of the analysis.
[a] Macular leakage area determined by fluorescein angiography. [b] The *P* value from the median 2-sample test is nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the *P* values. 95% CIs are shown. CI, confidence interval; Q8W, every 8 weeks; T&E, treat-and-extend. Presented by Tan CS at APAO February 22-25, 2023.

YOSEMITE/RHINE: Assessment of Hard Exudates on Colour Fundus Photography

Hard Exudate (HE) Grading

- Masked readers from Wisconsin Reading Centre assessed HEs within 6-mm ETDRS grid on CFP
- Performed at baseline and weeks 16, 52 and 96
- Grading of “definite” and “questionable” categorised as “presence” of HEs





[a] Primary efficacy endpoint: adjusted mean BCVA change from baseline at 1 year, averaged over weeks 48, 52, and 56. BCVA, best-corrected visual acuity; CFP, color fundus photography; D1, day 1; ETDRS, Early Treatment Diabetic Retinopathy Study; Q8W, every 8 weeks; T&E, treat-and-extend. Presented by Dinah C at EURETINA 2024

Case Report 2

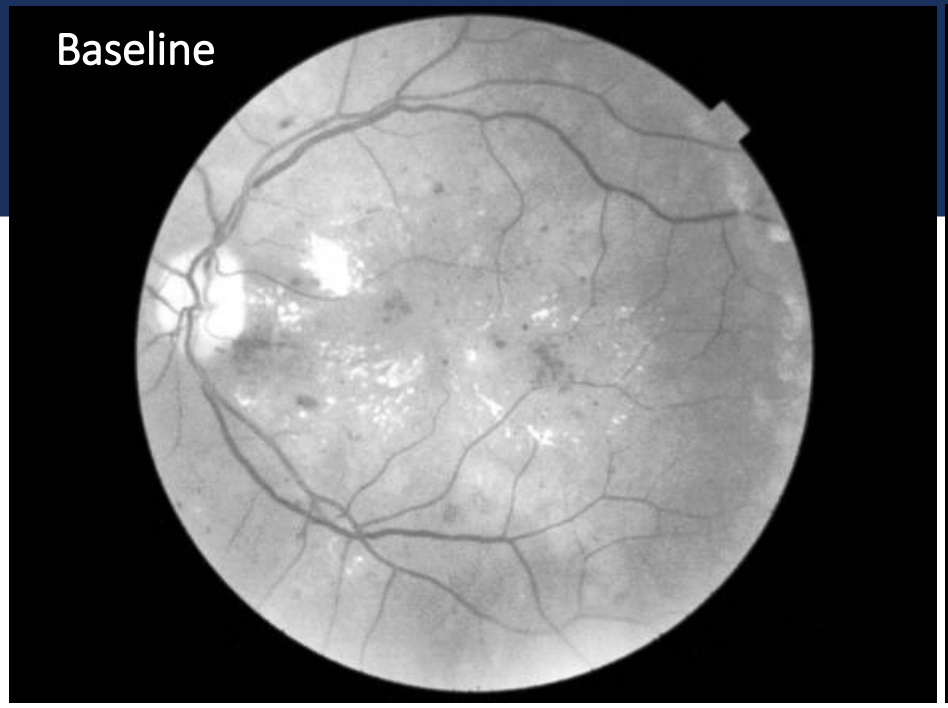
Patient history

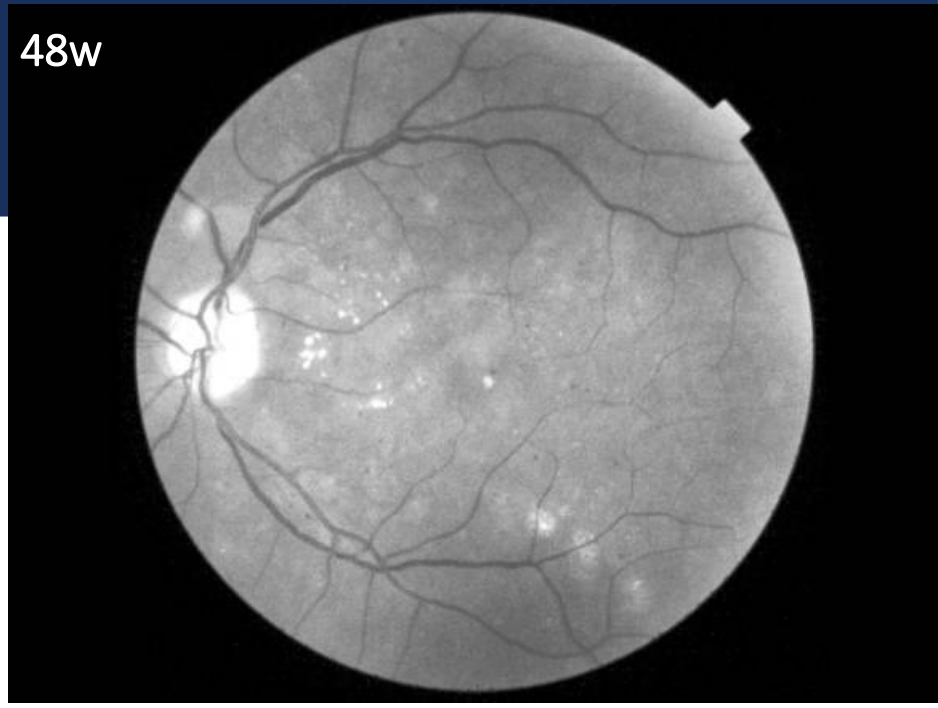
Age: 67

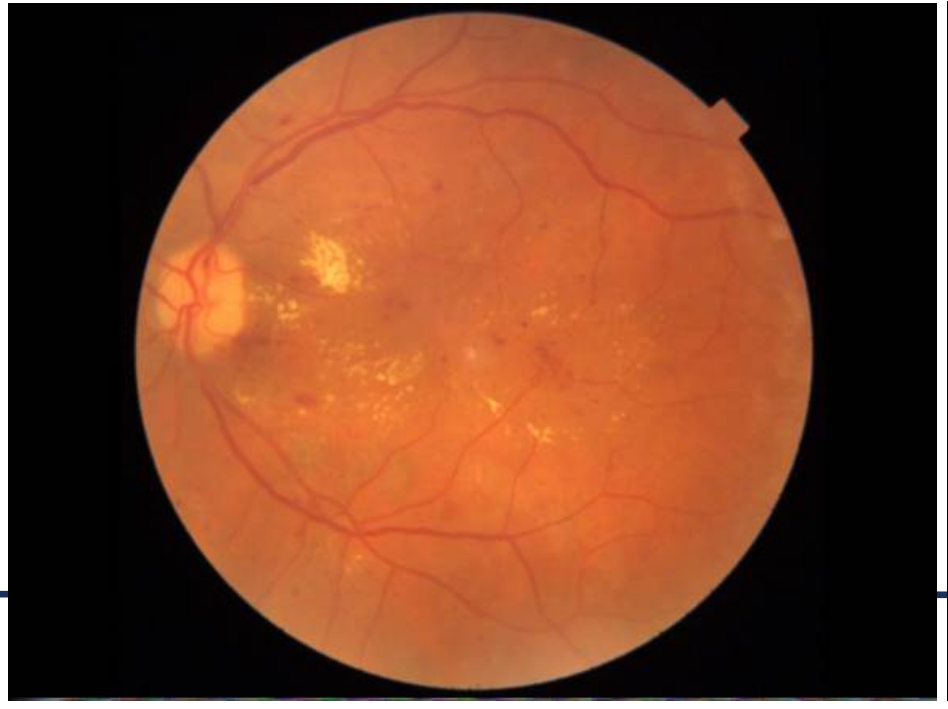
Sex: Female

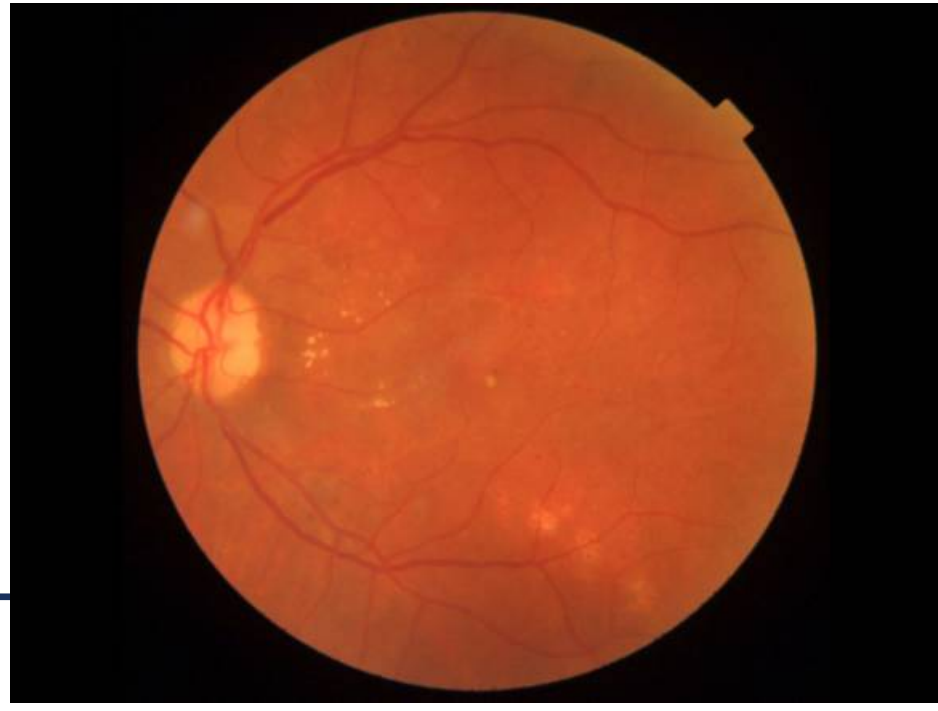
Diabetes duration: 9 years

Naïve diabetic macular edema

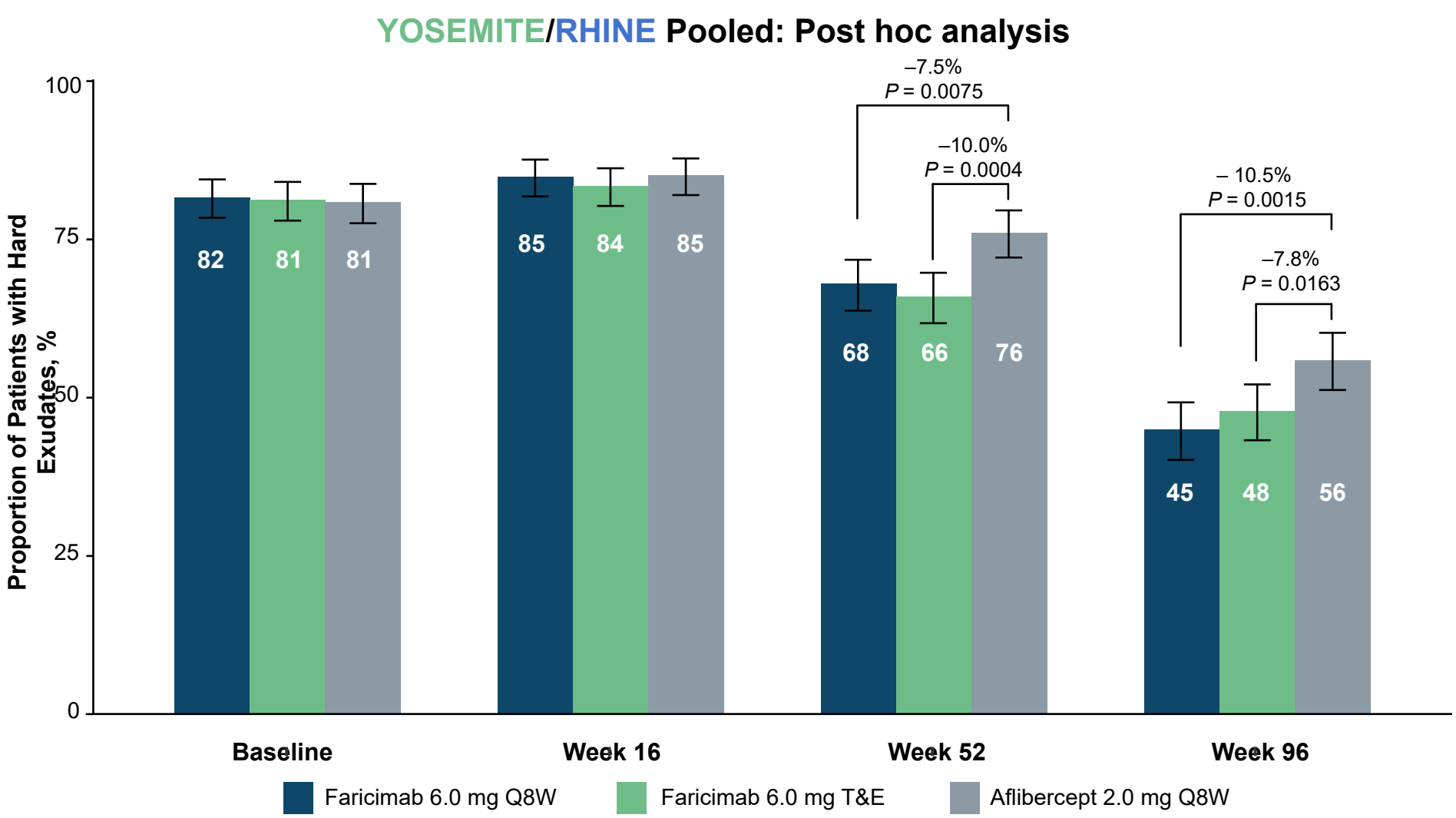








Fewer Patients with Hard Exudates After Faricimab vs Aflibercept at Week 52 and 96

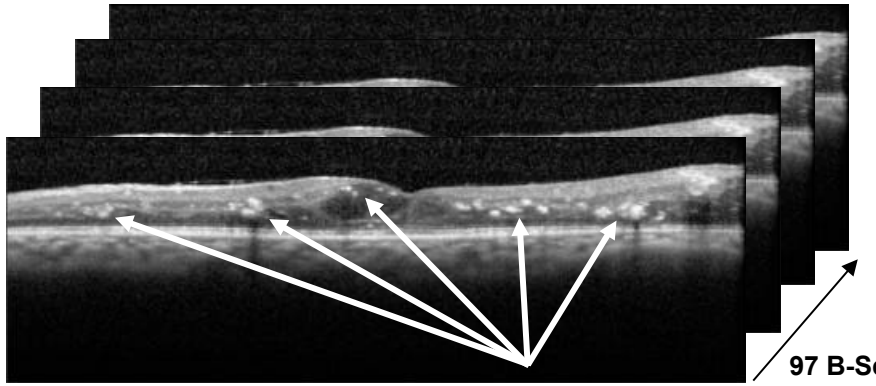


HE was evaluated at a central reading center using colour fundus photography. The weighted estimate is based on Cochran-Mantel-Haenszel test stratified by baseline BCVA score (< 64 letters vs ≥ 64 letters), prior intravitreal anti-VEGF therapy (yes vs no), region (US and Canada vs the rest of the world) and study (YOSEMITE vs RHINE). Missing data were not imputed. 95% CI is reported. Baseline is defined as the last available measurement obtained on or before randomisation. 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; Q8W, every 8 weeks; T&E, treat-and-extend; VEGF, vascular endothelial growth factor. Presented by Dinah C at EURETINA 2024

YOSEMITE/RHINE: Volumetric Assessment of Hard Exudates on OCT Using a Deep Learning-Based Algorithm

YOSEMITE/RHINE Pooled: Post Hoc Analysis

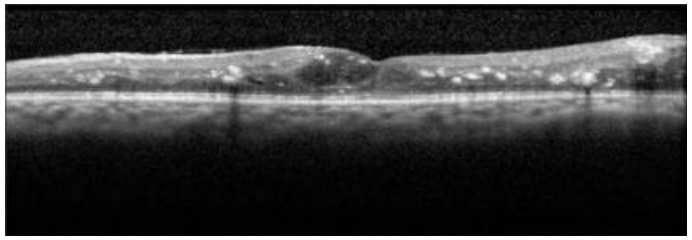
Whole SD-OCT volumes:



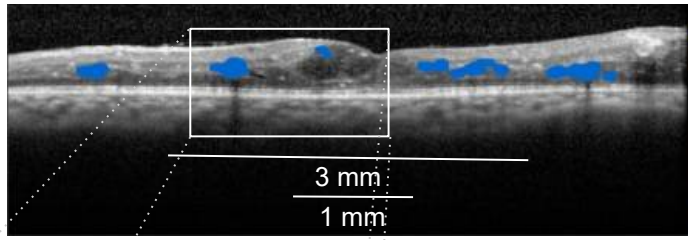
B-Scan with automated segmentation of hard exudates (> 50 µm)

Counts of hard exudate objects (on the B-scan level) and total hard exudate volumes were automatically extracted

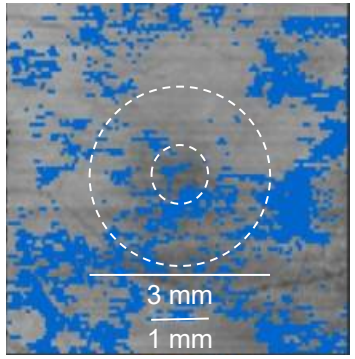
Original B-scan



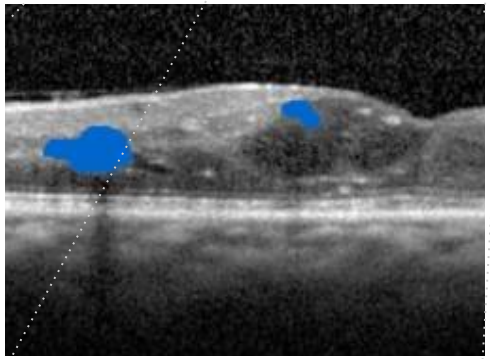
Post-processed result of hard exudate segmentation



En-face view



3-mm HE volume = 114 nL
3-mm HE count = 133

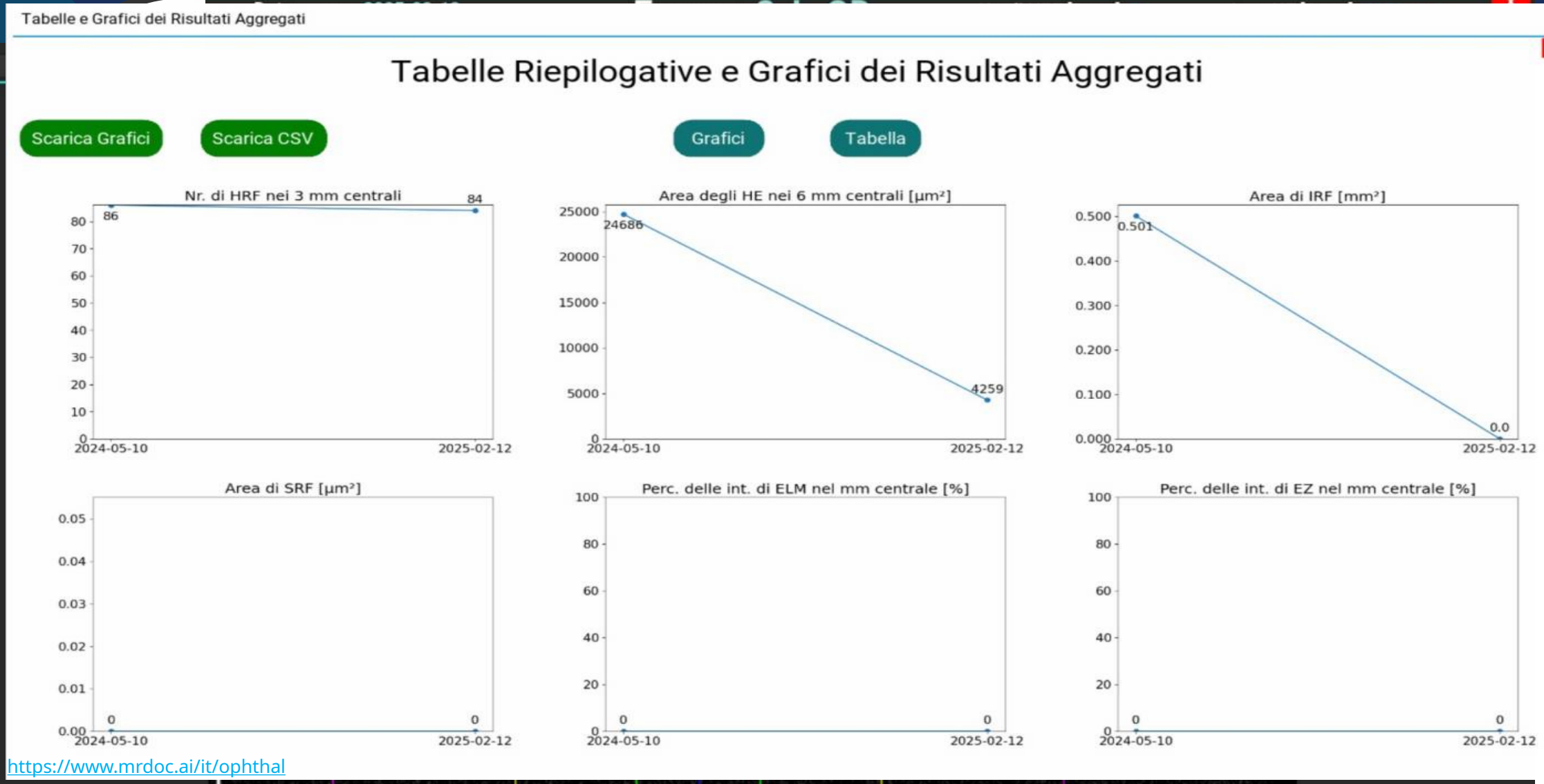


Total retina (ILM to RPE)

Blue = hard exudate (> 50 µm)

HE, hard exudate; ILM, internal limiting membrane; OCT, optical coherence tomography; RPE, retinal pigment epithelium; SD-OCT, spectral-domain optical coherence tomography. Presented by Dinah C at EURETINA 2024

AI in retinal diagnosis: Ophtal, Mr.Doc[1]

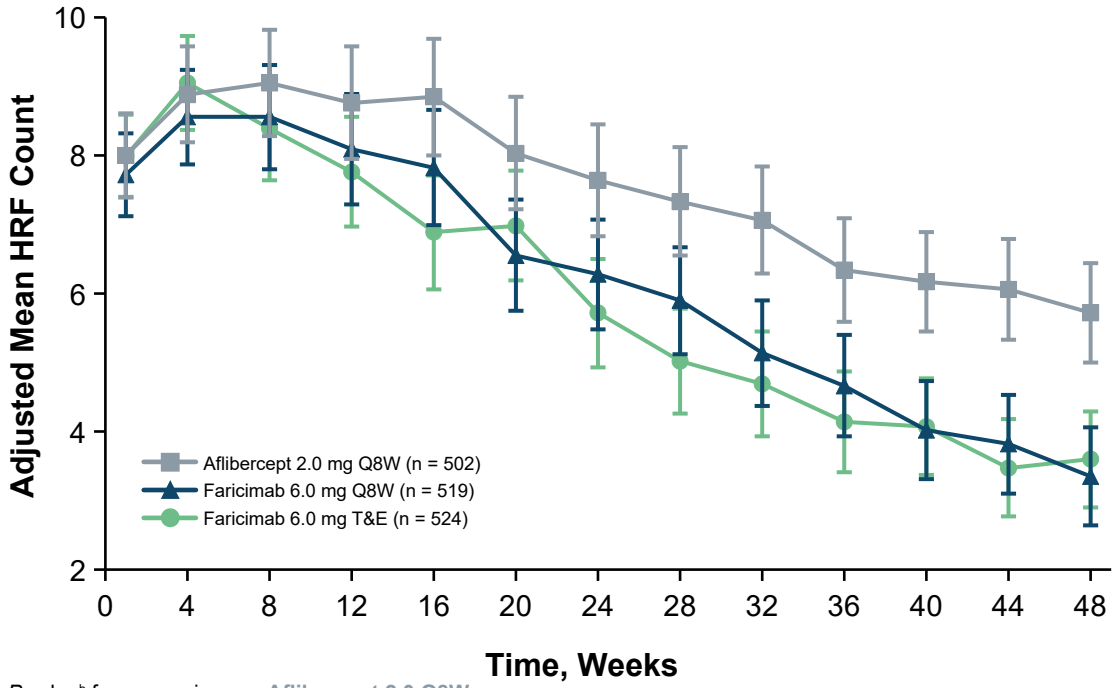


1. https://www.mrdoc.ai/it/ophthal

Greater Reductions in HRF Counts in the Inner Retina[a] With Faricimab vs Aflibercept Overtime

YOSEMITE/RHINE Pooled: Post Hoc Analysis

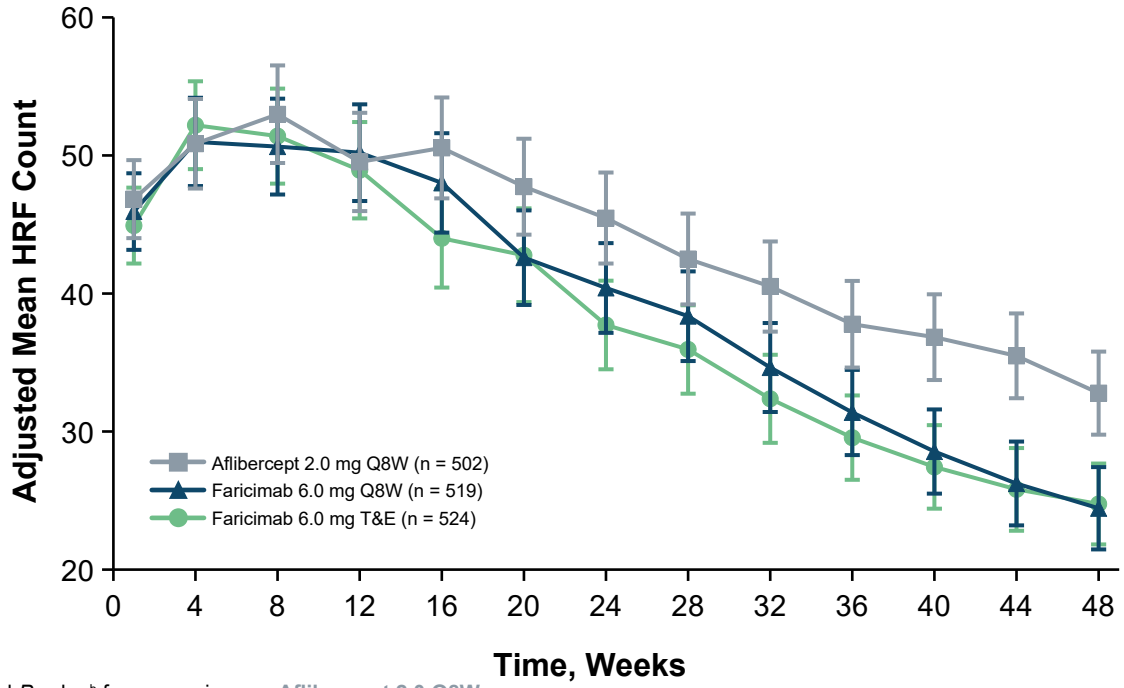
Inner Retina 1-mm Diameter



Nominal *P* value[b] for comparison vs Aflibercept 2.0 Q8W

Faricimab Q8W	0.472	0.474	0.332	0.218	0.072	**0.007**	**0.012**	**0.006**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Faricimab T&E	0.986	0.711	0.197	0.066	<0.001	0.053	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**

Inner Retina 3-mm Diameter



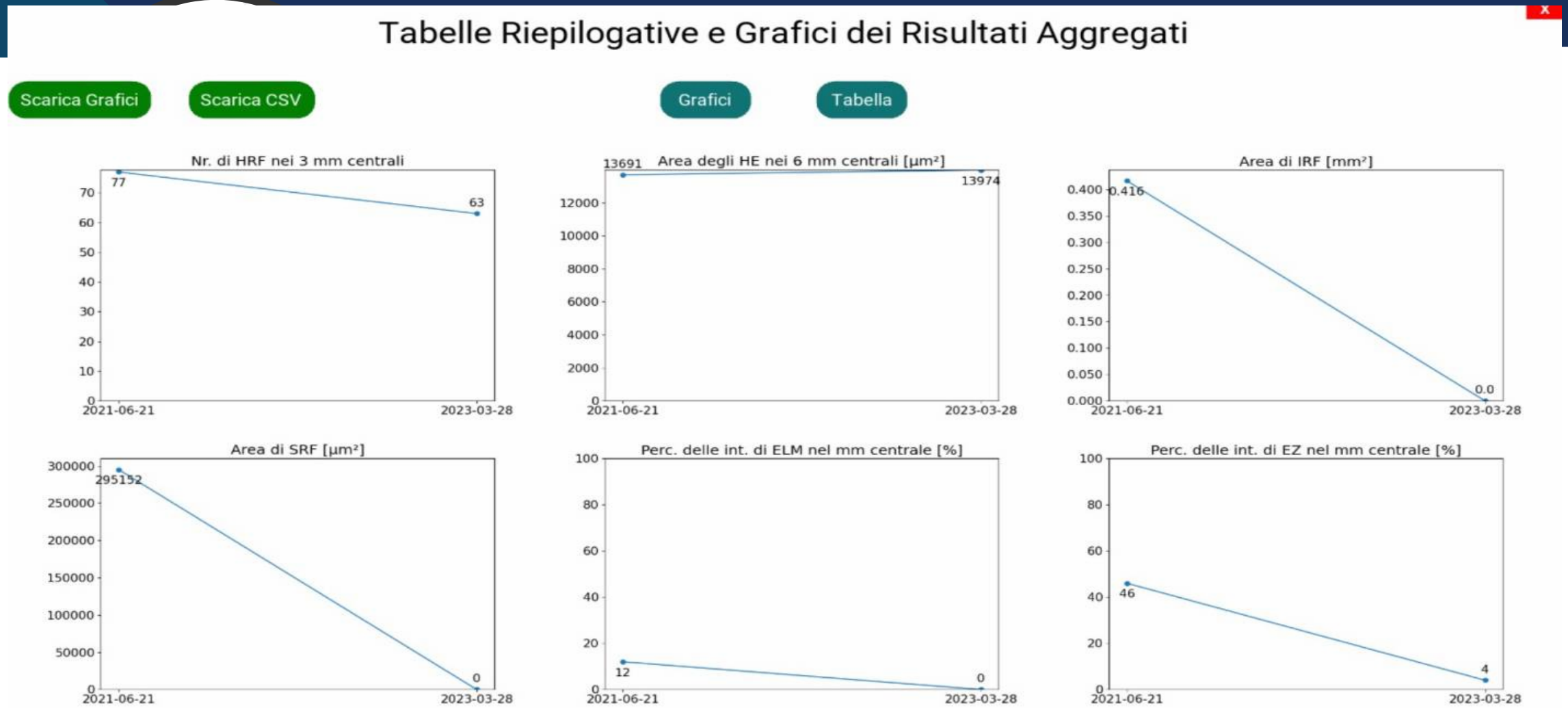
Nominal *P* value[b] for comparison vs Aflibercept 2.0 Q8W

Faricimab Q8W	0.617	0.951	0.319	0.778	0.300	**0.026**	**0.020**	0.056	**0.006**	**0.002**	**<0.001**	**<0.001**	**<0.001**
Faricimab T&E	0.285	0.528	0.499	0.801	**0.007**	**0.031**	**<0.001**	**0.002**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**

Similar results were seen in the **outer retina**

[a] ILM to OPL-HFL. [b] *P* values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the *P* values.
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.
CI, confidence interval; HFL, Henle's fibre layer; HRF, hyperreflective foci; ILM, internal limiting membrane; OPL, outer plexiform layer; Q8W, every 8 weeks; T&E, treat-and-extend. Presented by Chakravarthy U at EURETINA 2023

AI in retinal diagnosis: Ophtal, Mr.Doc[1]



1. https://www.mrdoc.ai/it/ophthal

Faricimab in DME: RHONE-X Long-Term Extension Trial

M-IT-00003954

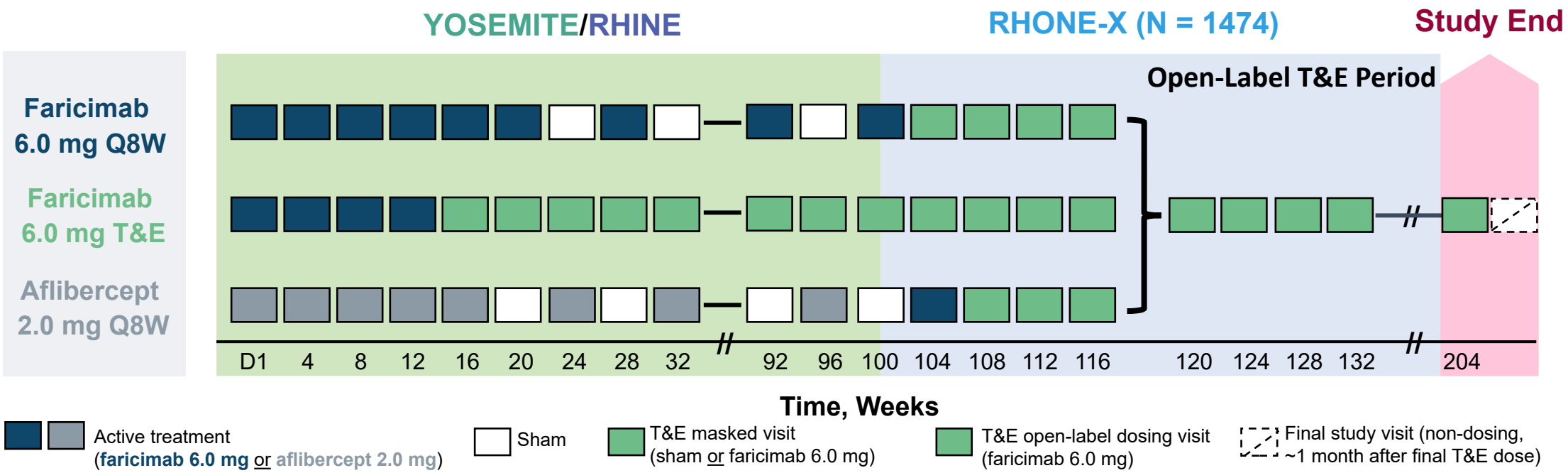
RHONE-X Extension Trial Assessed the Long-Term Safety and Efficacy of Faricimab Treat & Extend in Patients With DME

Phase 3, multicentre, open-label, long-term extension trial

- Patients with DME who completed 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

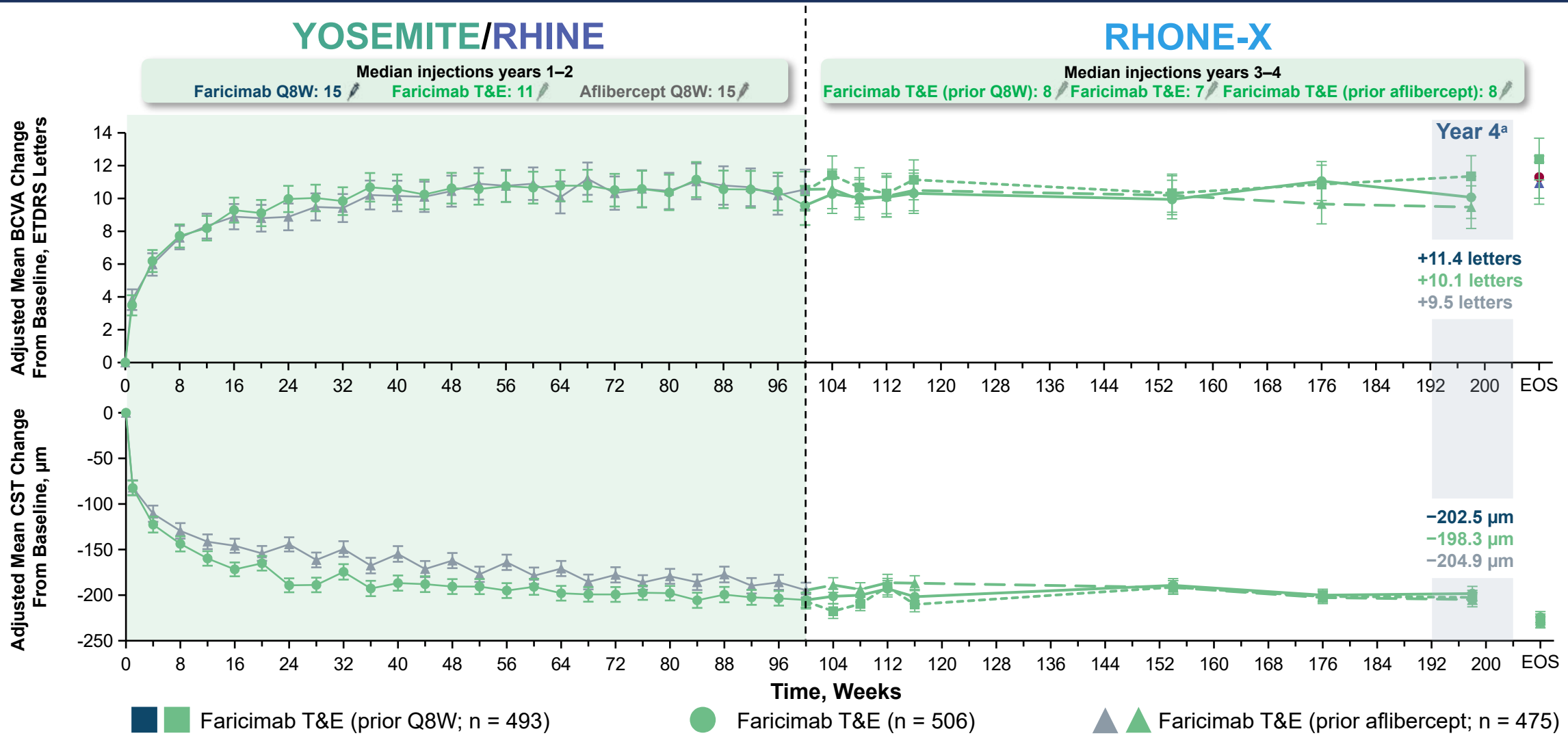
Faricimab treat & extend in RHONE-X

- **Extend** (by 4 weeks, max Q16W) if stable **CST AND BCVA**
- **Reduce** (by 4 or 8 weeks, min Q4W) if worsening **CST ± BCVA**
- **Maintain** if extension or reduction criteria not met



YOSEMITE (NCT03622580); RHINE (NCT03622593); RHONE-X (NCT04432831). Personalised 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; Q4W, every 4 weeks; Q8W, every 8 weeks; Q16W, every 16 weeks; T&E, treat-&-extend. Presented by Schlottmann P at EURETINA 2024

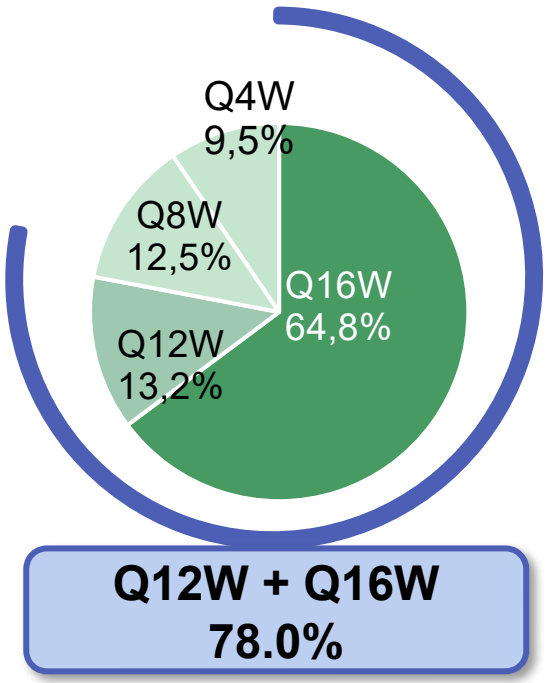
Robust Vision Gains and Improved CST Achieved During YOSEMITE/RHINE Were Maintained in RHONE-X With Faricimab up to Q16W Dosing



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. [a] Adjusted mean change from baseline at year 4 of RHONE-X, averaged over weeks 192 to 204. Estimates for year 3 and 3.5 are averaged over weeks 144 to 164 and 168 to 188, respectively. 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. Presented by Schlottmann P at EURETINA 2024

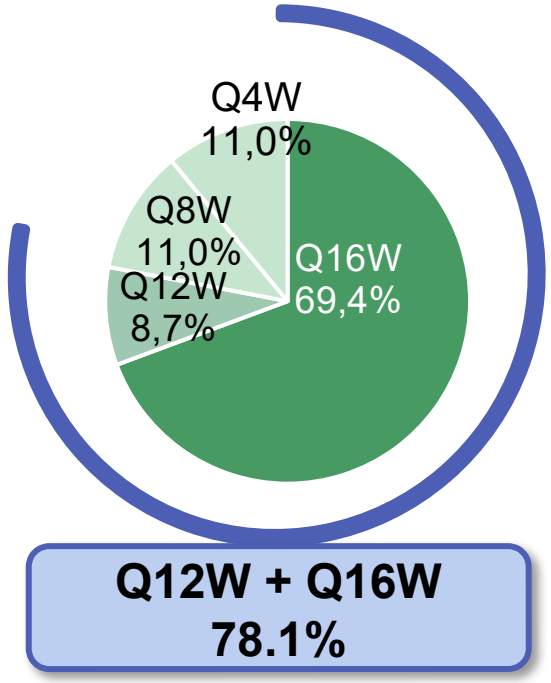
Approximately 80% of Patients Were on Extended Dosing (Q16W or Q12W) at the End of 4 Years

Faricimab T&E (prior Q8W) (n = 440)



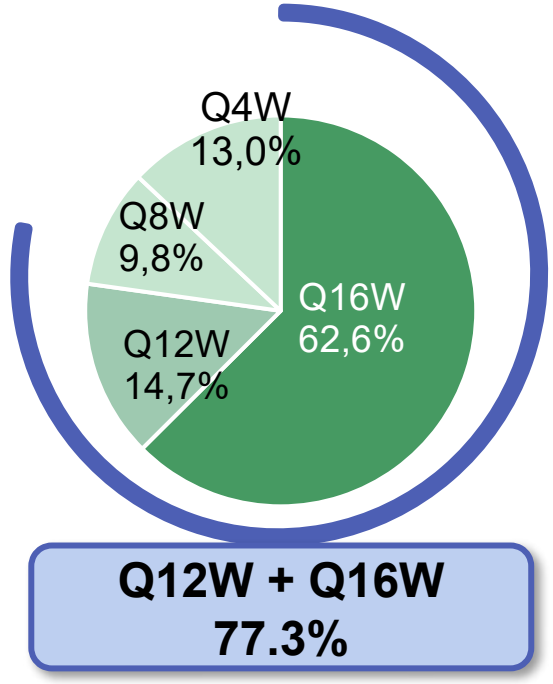
Q12W + Q16W 78.0%

Faricimab T&E (n = 438)



Q12W + Q16W 78.1%

Faricimab T&E (prior aflibercept) (n = 409)

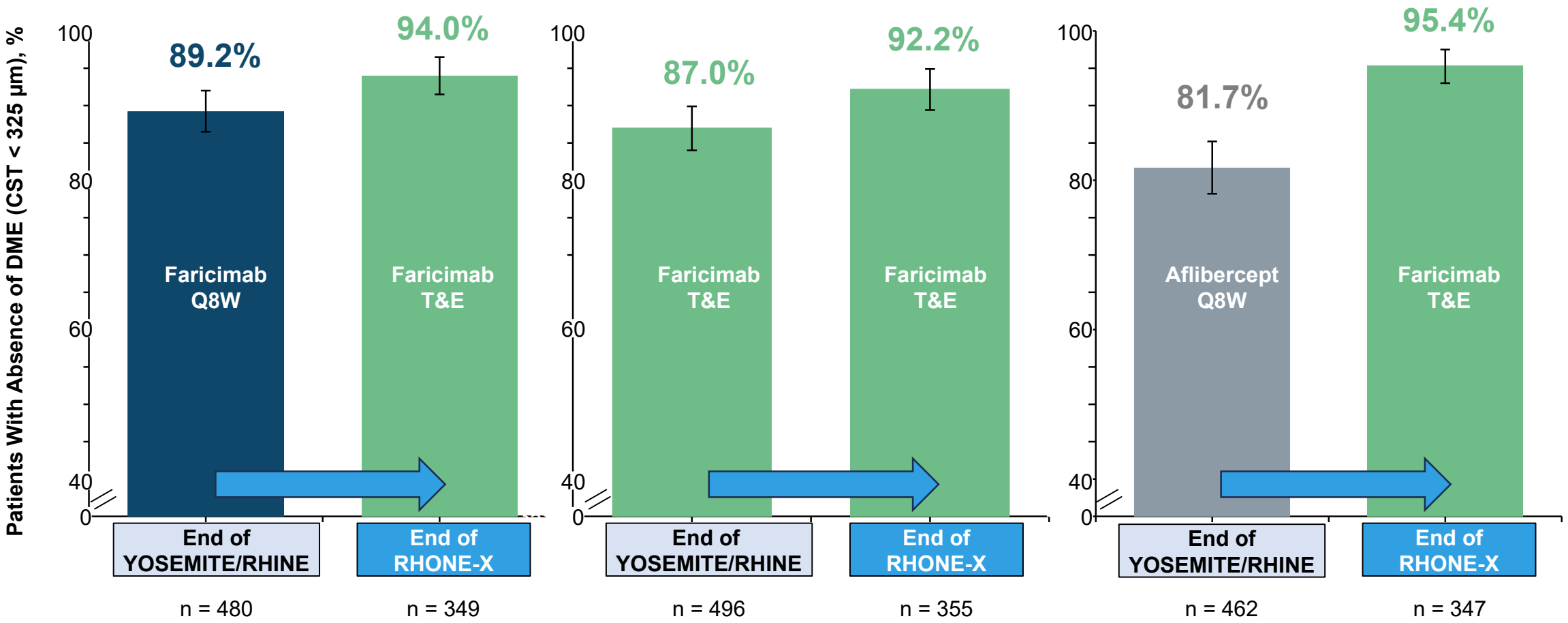


Q12W + Q16W 77.3%

Proportion of patients included in the study on Q4W, Q8W, Q12W or Q16W dosing at year 4 among those who had not discontinued the study at year 4. Treatment interval was defined as the treatment interval decision followed at year 4. The last observed T&E in the visit window for year 4 (weeks 192 to 204) is used as the patient's T&E at that time point. Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks; T&E, treat-and-extend.

Presented by Schlottmann P at EURETINA 2024

Absence of DME Was Achieved by > 90% of Patients by the End of RHONE-X Regardless of Prior Treatment Arm



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. End of YOSEMITE/RHINE is week 100/day 1 of RHONE-X and end of RHONE-X is final study visit (minimum of 28 days after the final faricimab dose). 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 (US 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. BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; CST, central subfield thickness; DME, diabetic macular edema; Q8W, every 8 weeks; T&E, treat-and-extend; VEGF, vascular endothelial growth factor. Presented by Schlottmann P at EURETINA 2024

Faricimab Was Well Tolerated Through Years 3 and 4 of RHONE-X With the Nature of AEs Consistent With the YOSEMITE/RHINE Parent Trials

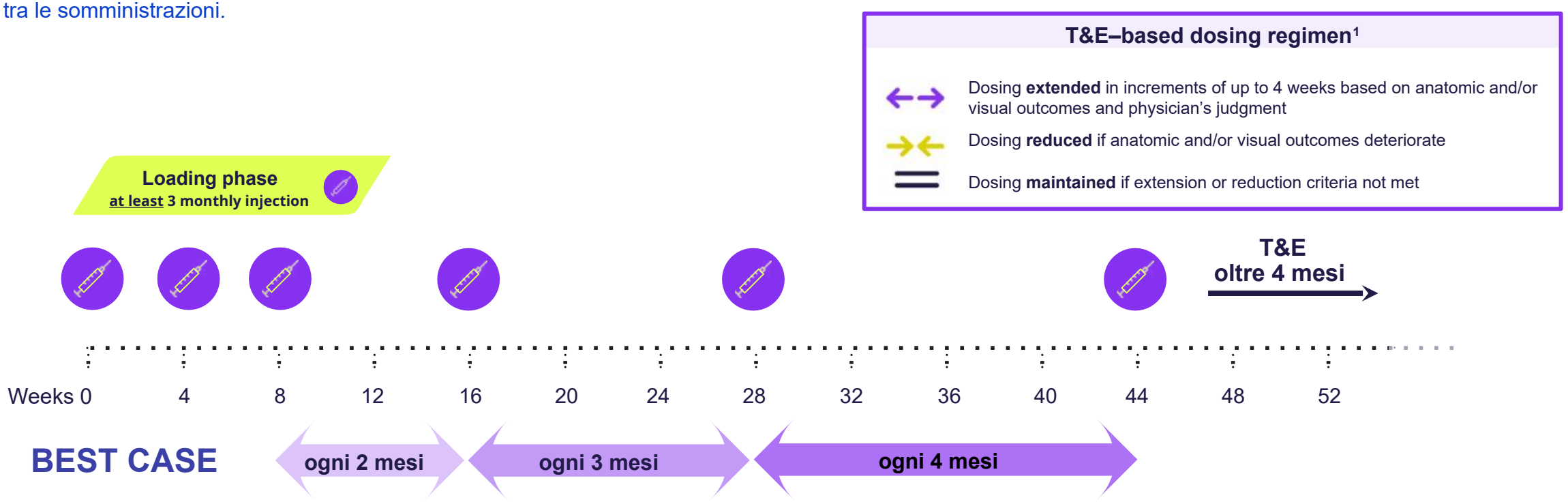
	RHONE-X		
AEs Through Study End, Patients With ≥ 1 AE, n (%)[a]	**Faricimab T&E (prior Q8W) n = 491**	**Faricimab T&E n = 500**	**Faricimab T&E (prior aflibercept) n = 473**
Ocular AEs[b]	219 (44.6%)	188 (37.6%)	197 (41.6%)
Serious ocular AEs[b]	31 (6.3%)	15 (3.0%)	26 (5.5%)
Ocular AEs of special interest[c]	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; Q8W, every 8 weeks. Presented by Schlottmann P at EURETINA 2024

Riassunto delle caratteristiche del prodotto

Posologia DME

La dose raccomandata è di 6 mg (0,05 mL di soluzione) somministrata attraverso **iniezione intravitreale ogni 4 settimane (una volta al mese). Possono essere necessarie 3 o più iniezioni mensili consecutive.** Successivamente, il trattamento viene personalizzato secondo l'approccio "trattare ed estendere" ***(treat-and-extend)***. Sulla base della valutazione clinica degli esiti anatomici e/o visivi del paziente, **l'intervallo di somministrazione può essere esteso fino a 4 settimane**. Se gli esiti anatomici e/o visivi cambiano, l'intervallo di trattamento deve essere, di conseguenza, adeguato e, se gli esiti anatomici e/o visivi peggiorano, si deve procedere alla riduzione dell'intervallo (vedere paragrafo 5.1). Non sono stati studiati intervalli di trattamento tra le somministrazioni inferiori a 4 settimane e maggiori di 4 mesi. Le visite di monitoraggio tra le somministrazioni devono essere pianificate sulla base dello stato del paziente e a discrezione del medico; tuttavia, non vi è obbligo di monitoraggio mensile tra le somministrazioni.



[1] https://www.ema.europa.eu/en/documents/product-information/vabysmo-epar-product-information_en.pdf