Extended Treatment Outcomes and the Potential for Q20W Dosing With Faricimab in Patients With DME: A Post Hoc Analysis of YOSEMITE/RHINE

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On behalf of the YOSEMITE and RHINE Investigators

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Disclosures

Financial Disclosures

- YM: Consultant: Alcon, Allergan, Alimera, Apellis, Bausch + Lomb, Dutch Ophthalmic Research Center, EyePoint, Genentech, Inc., Iveric Bio, Regeneron, Thea, ZEISS
- MA: Consultant: Genentech, Inc., NorthGauge Healthcare Advisors, Regeneron; Speaker: Apellis, Genentech, Inc., Iveric Bio, Regeneron
- KG: Employee: F. Hoffmann-La Roche Ltd.
- DS, MA: Employee: Genentech, Inc.
- LH: Consultant: Alimera, Genentech, Inc.
- MS: Consultant: Aerie, Allegro, Allergan, EyePoint, Genentech, Inc., Kodiak Sciences, Novartis, Regeneron, Santen; Speaker: Allergan, Genentech, Inc., Mallinckrodt, Novartis, Regeneron, Spark; Contracted Research: Aerie, Allegro, Allergan, DRCR.net, Genentech, Inc., Icon, Ionis, KalVista, Kodiak Sciences, Novartis, Opthea, Optos, Regeneron, Ribomic, Santen, Senju, Sydnexis; Equity: Aviceda, Inflammasome, Nanoscope

Study and Product Disclosures

- Faricimab is approved for the treatment of neovascular age-related macular degeneration, diabetic macular edema, and retinal vein occlusion in multiple countries worldwide. Faricimab is not currently approved for use outside these indications
- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
- Funding was provided by F. Hoffmann-La Roche Ltd. for the study and third-party writing assistance, which was provided by Nicole Tom, PhD, of Envision Pharma Group

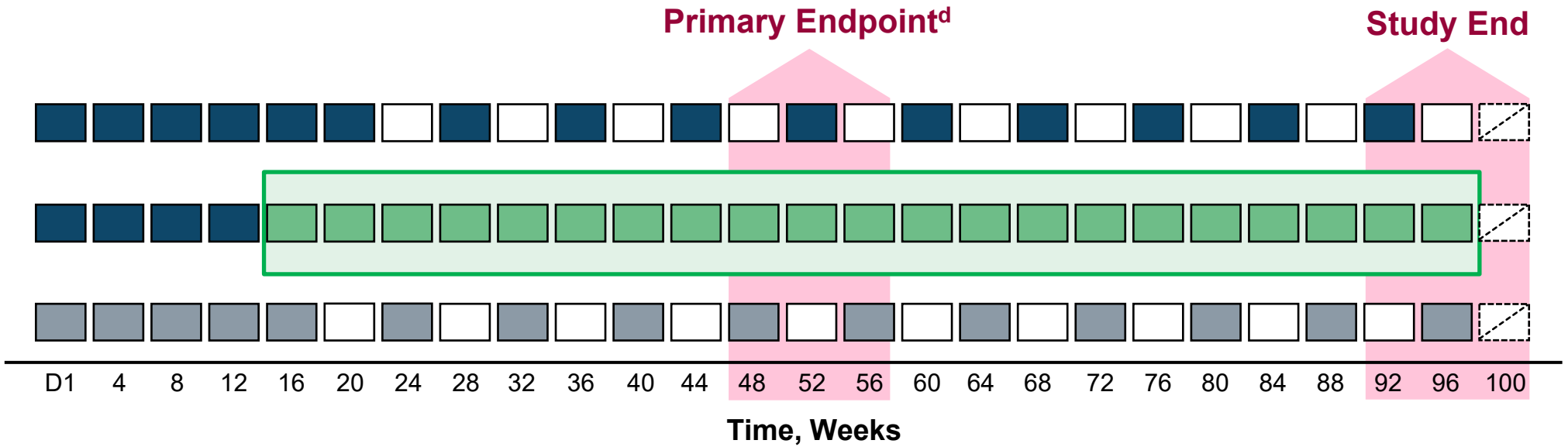
YOSEMITE and RHINE Trial Design

Treatment-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]

Faricimab 6.0 mg Q8W

Faricimab 6.0 mg T&E

Aflibercept 2.0 mg Q8W



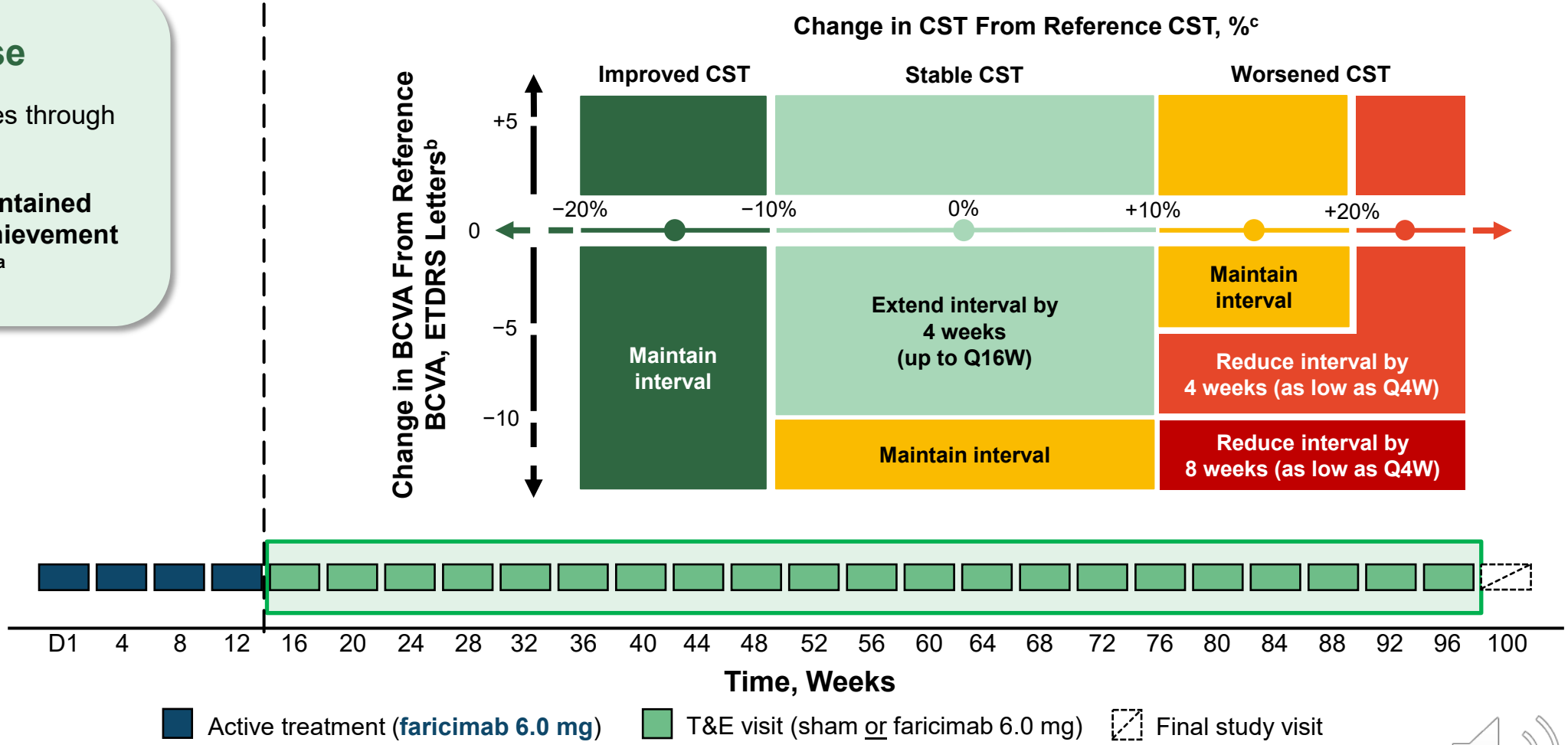
YOSEMITE (NCT03622580); RHINE (NCT03622593). [a] Previously anti-VEGF–treated eyes (treated ≥ 3 months before day 1) were limited to 25% of the total enrollment. [b] CST was measured as the distance from the ILM to Bruch's membrane. [c] BCVA was measured using the ETDRS VA chart at a starting distance of 4 m. [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; ILM, internal limiting membrane; Q8W, every 8 weeks; T&E, treat-and-extend; VA, visual acuity; VEGF, vascular endothelial growth factor.

Faricimab DME Trials Use Disease Criteria Reflective of Clinical Practice

Initiation Phase

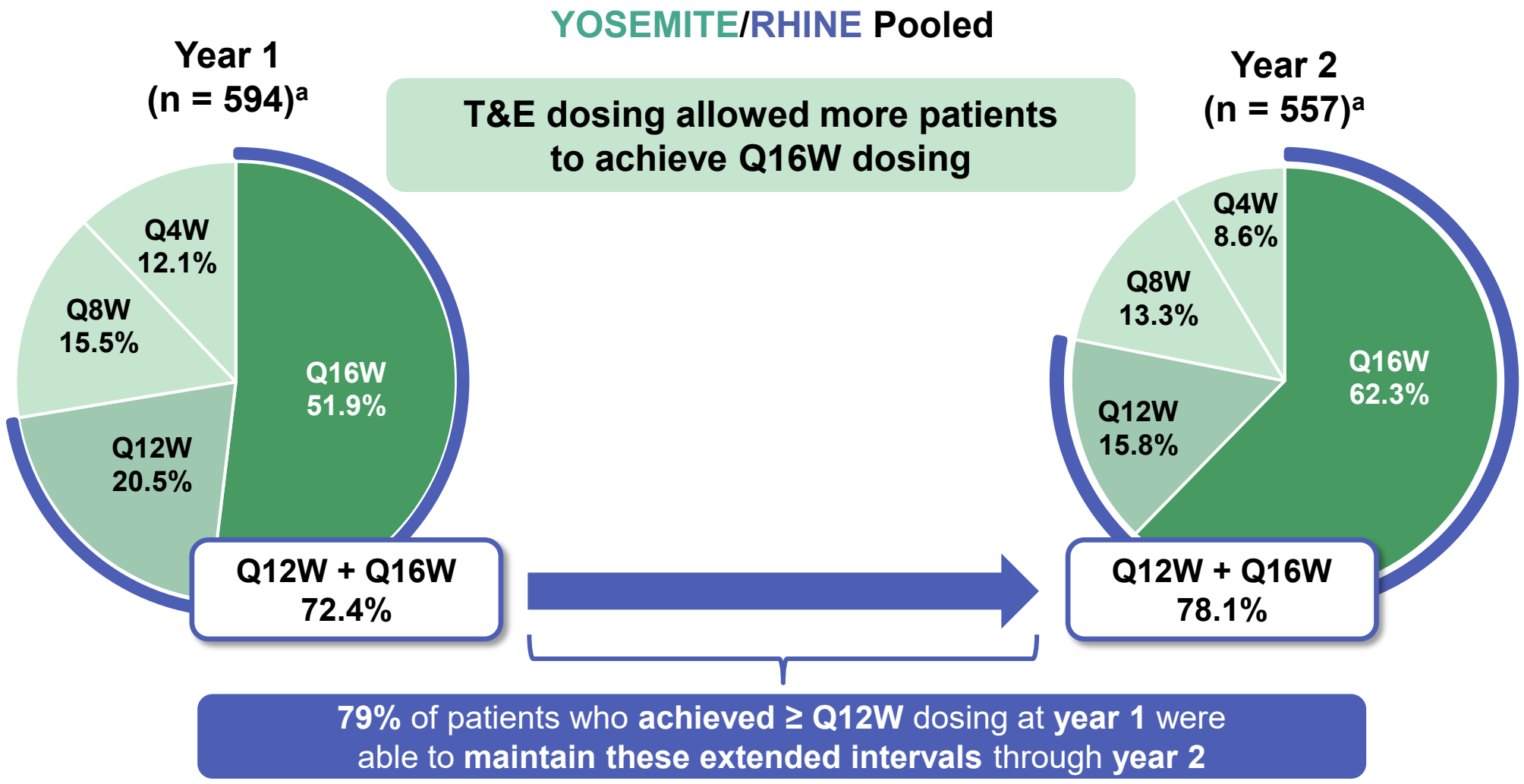
- 4 initial Q4W doses through week 12
- **Q4W dosing maintained until the first achievement of CST < 325 µm[a]**

Personalized T&E Phase



YOSEMITE (NCT03622580); RHINE (NCT03622593). [a] CST was measured as the distance from the ILM to Bruch's membrane. [b] Reference BCVA was defined as the mean of the 3 best BCVA values achieved at any prior active dosing visit. [c] Reference CST was defined as the CST value when the original reference value (CST < 325 µm) was achieved. Reference CST was adjusted if CST decreased by > 10% from the previous reference CST for 2 consecutive active dosing visits and the values obtained were within 30 µm. The CST value obtained at the latter visit served as the new reference CST.
BCVA, best-corrected visual acuity; CST, central subfield thickness; D, day; DME, diabetic macular edema; ETDRS, Early Treatment Diabetic Retinopathy Study; ILM, internal limiting membrane; Q4W, every 4 weeks; Q16W, every 16 weeks; T&E, treat-and-extend.

~80% of Faricimab-Treated Patients Achieved ≥ Q12W Dosing at the End of the Second Year



[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.
Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks; T&E, treat-and-extend.

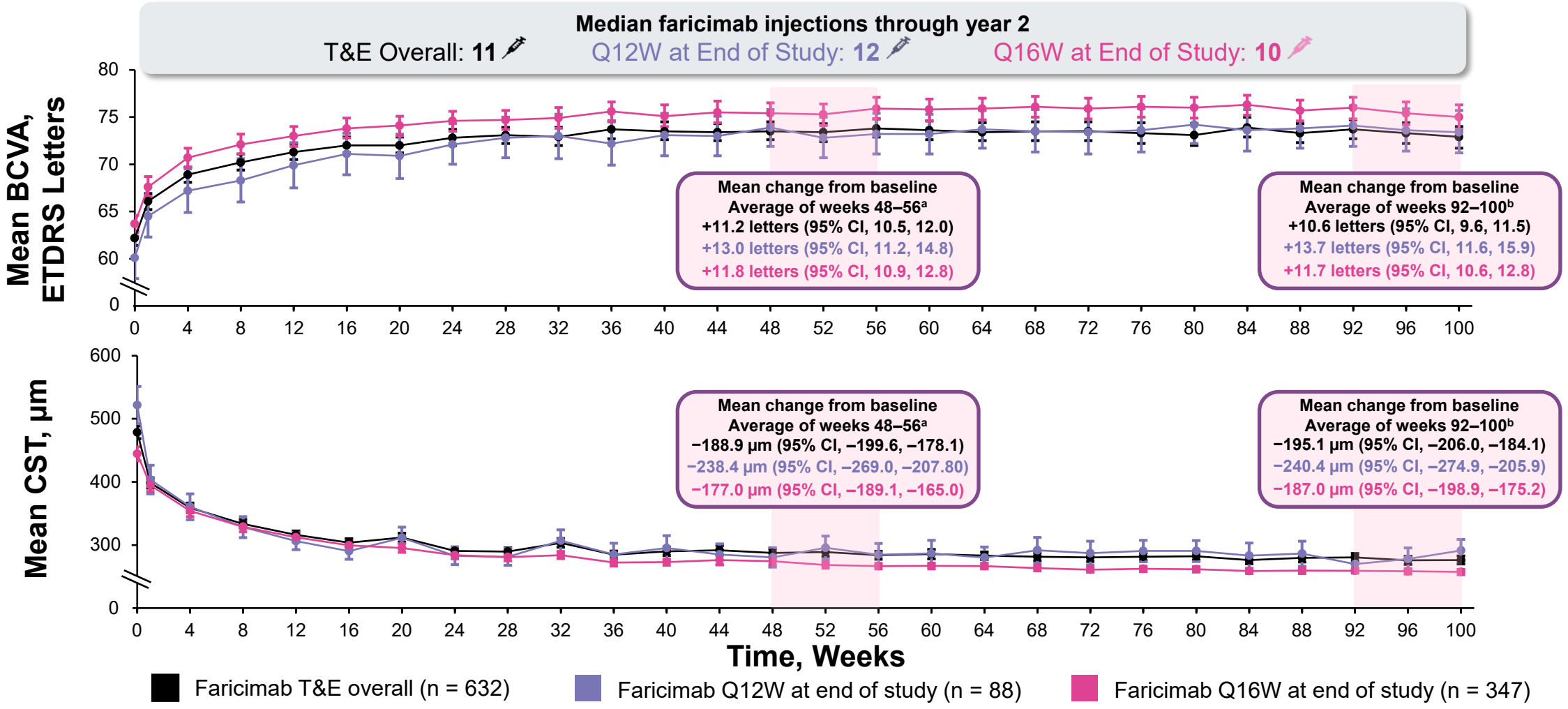
Baseline Patient Characteristics

Characteristic	Faricimab T&E Overall N = 632	Faricimab Q12W at End of Study N = 88	Faricimab Q16W at End of Study N = 347
Age, years, mean (SD)[a]	62.2 (10.1)	62.1 (9.8)	62.0 (10.3)
Female, n (%)	236 (37.3)	33 (37.5)	121 (34.9)
Race, n (%)			
White	489 (77.4)	68 (77.3)	270 (77.8)
Black or African American	48 (7.6)	4 (4.5)	30 (8.6)
Asian	62 (9.8)	12 (13.6)	33 (9.5)
American Indian or Alaska Native	5 (0.8)	2 (2.3)	2 (0.6)
Hispanic, n (%)	118 (18.7)	11 (12.5)	63 (18.2)
BCVA, letters, mean (SD)	62.2 (9.8)	60.1 (10.6)	63.7 (8.5)
CST, µm, mean (SD)[b]	478.5 (129.0)	521.8 (138.2)	444.7 (105.3)
Previously anti-VEGF treated, n (%)	133 (21.0)	24 (27.3)	57 (16.4)
Months since DME diagnosis, mean (SD)	19.1 (34.7)	24.5 (48.7)	18.2 (34.3)
Macular ischaemic nonperfusion, n (%)	242 (41.2)	33 (39.8)	133 (40.4)

[a] Age at randomization. [b] CST was measured as the distance from the ILM to Bruch's membrane. Grouping by faricimab dosing interval at end of study were performed retrospectively.
BCVA, best-corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; ILM, internal limiting membrane; Q12W, every 12 weeks; Q16W, every 16 weeks; SD, standard deviation; T&E, treat-and-extend; VEGF, vascular endothelial growth factor.

Robust and Stable Vision and CST Improvements Through 2 Years in Patients on Q12W or Q16W Dosing at Week 96

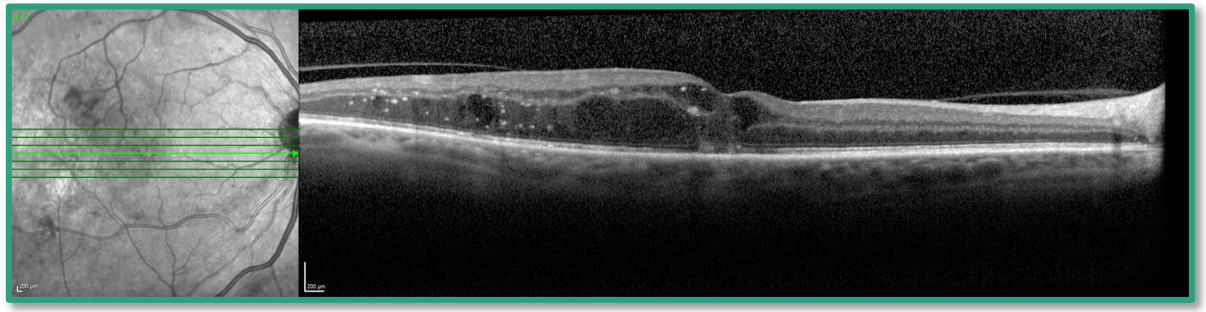
YOSEMITE/RHINE Pooled: Post Hoc Analysis



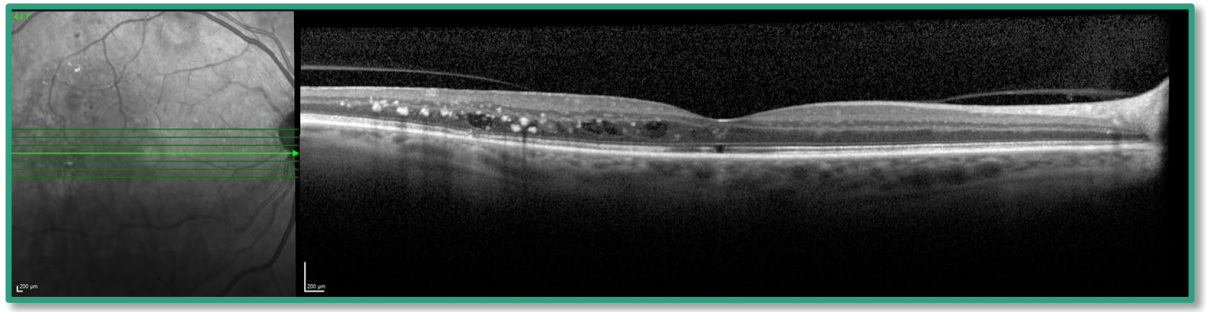
Patients were analyzed as randomized (ITT principle) and were included in the analysis through completion/discontinuation. Baseline is defined as the last available value on or prior to randomization. 95% CIs are shown. The median number of injections is based on the safety-evaluable population. CST was measured as ILM-RPE, as graded by central reading center. BCVA, best-corrected visual acuity; CI, confidence interval; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intent to treat; Q12W, every 12 weeks; Q16W, every 16 weeks; T&E, treat-and-extend.

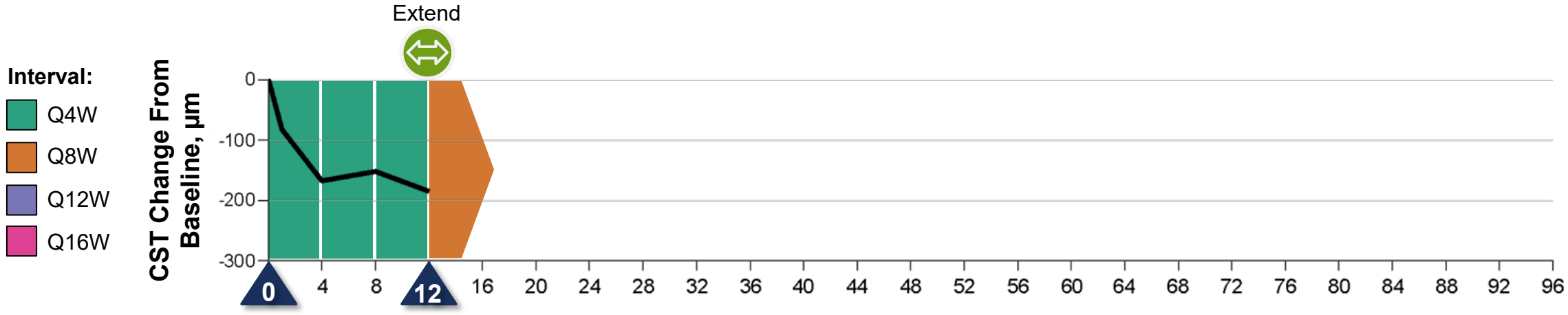
Trial Case:
Rapid Extension to Q16W Dosing, Maintained Through Year 2

Baseline (day 1):
BCVA 57 ETDRS letters
CST 489 µm



Week 12:
BCVA 81 ETDRS letters
CST 304 µm





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

BCVA, best-corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intent to treat; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks.

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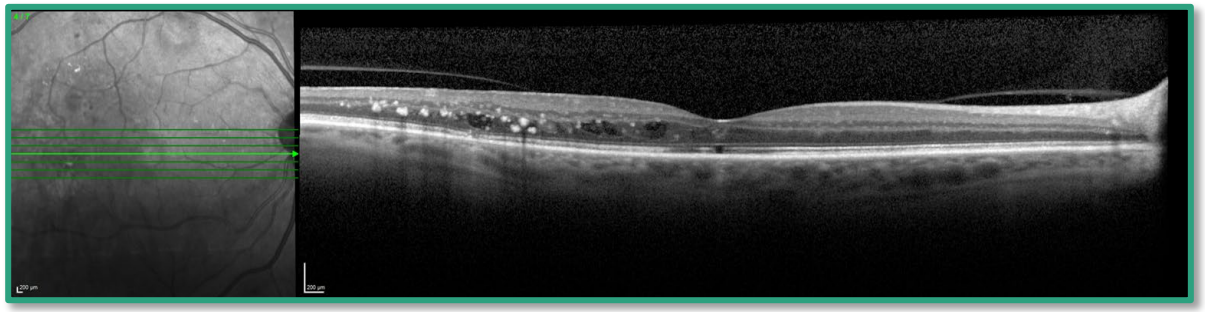
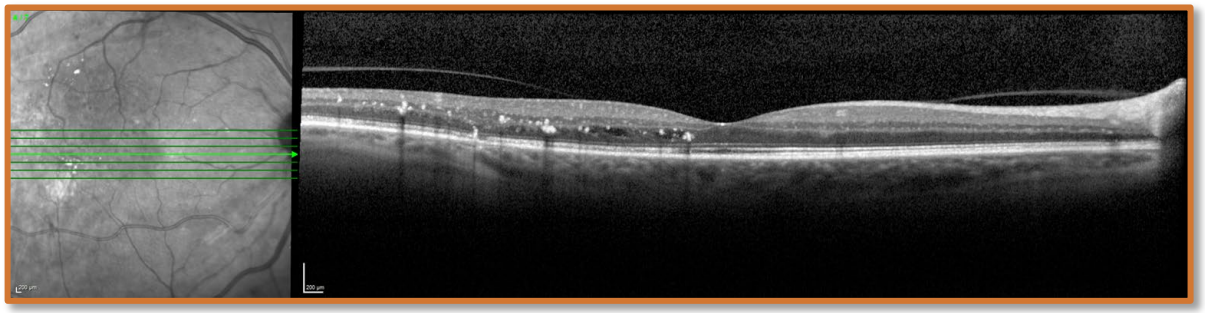
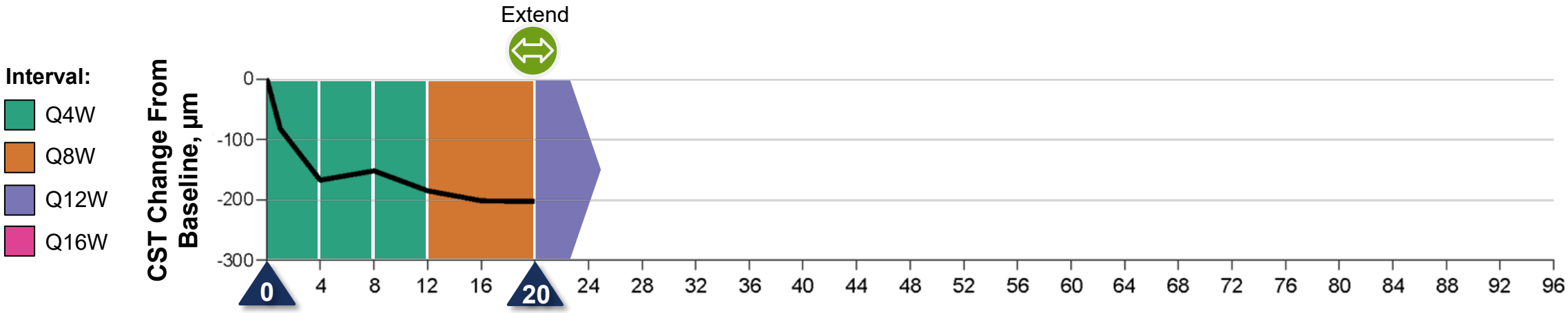


Week 20:
BCVA 85 ETDRS letters
CST 286 µm





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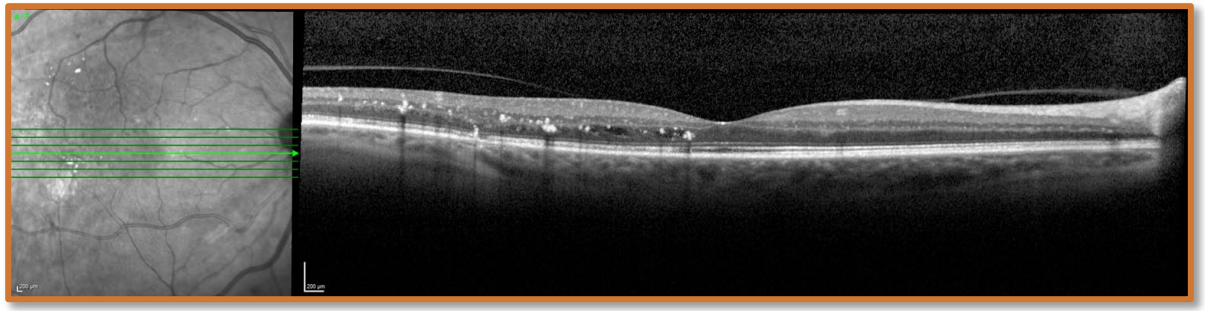
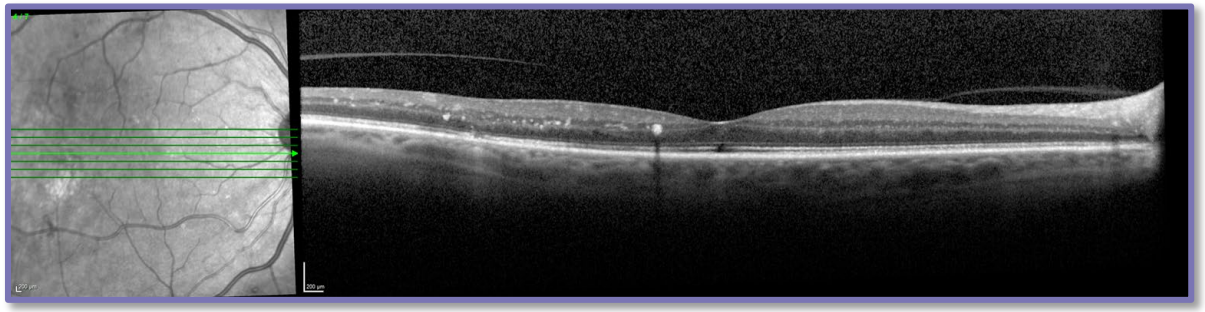
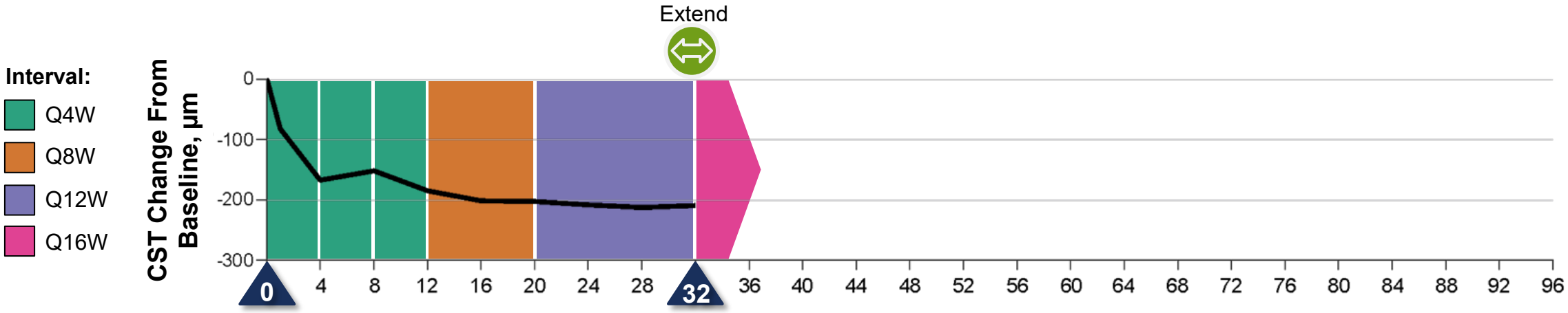


Week 32:
BCVA 77 ETDRS letters
CST 280 µm





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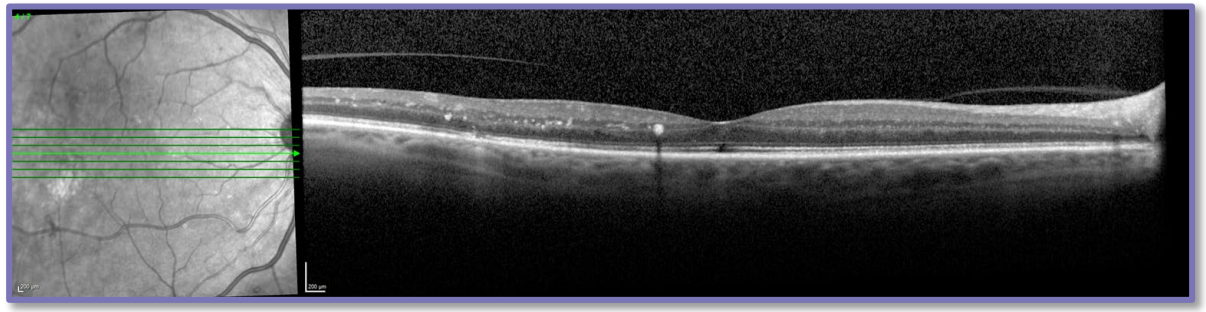
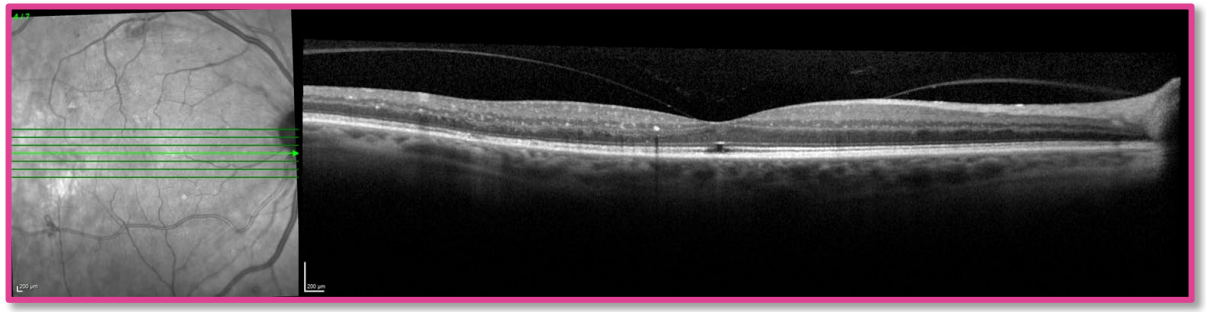
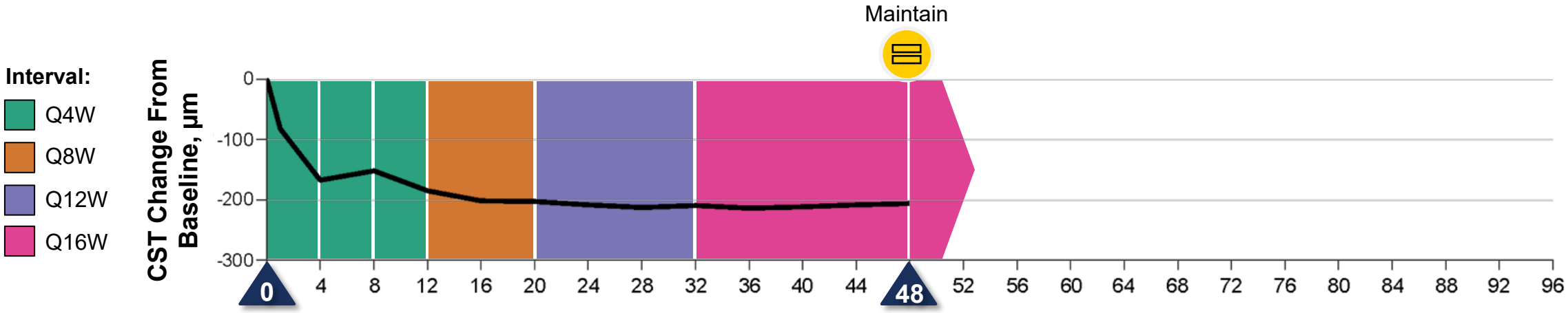


Week 48:
BCVA 82 ETDRS letters
CST 283 µm





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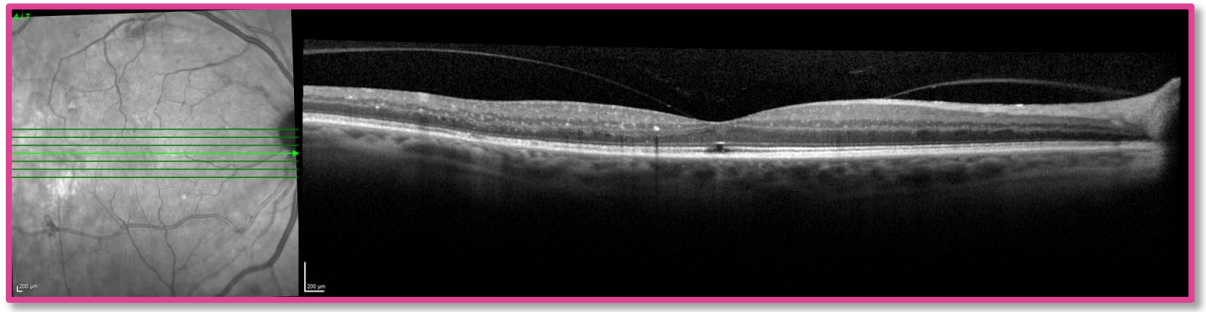
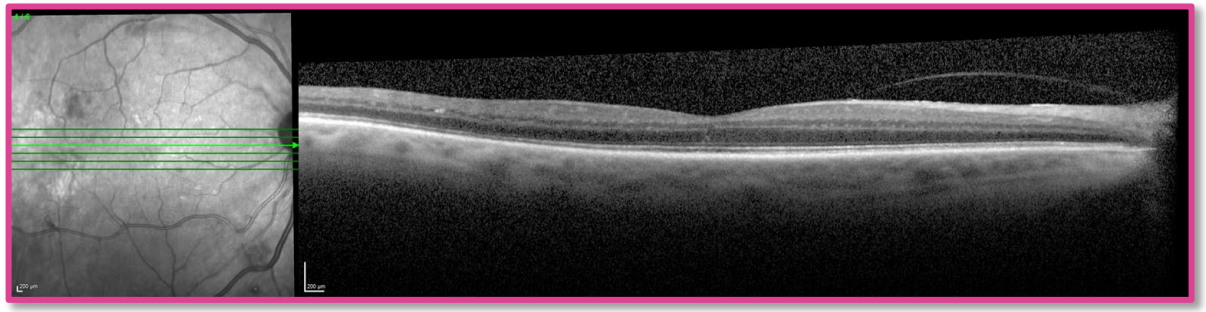
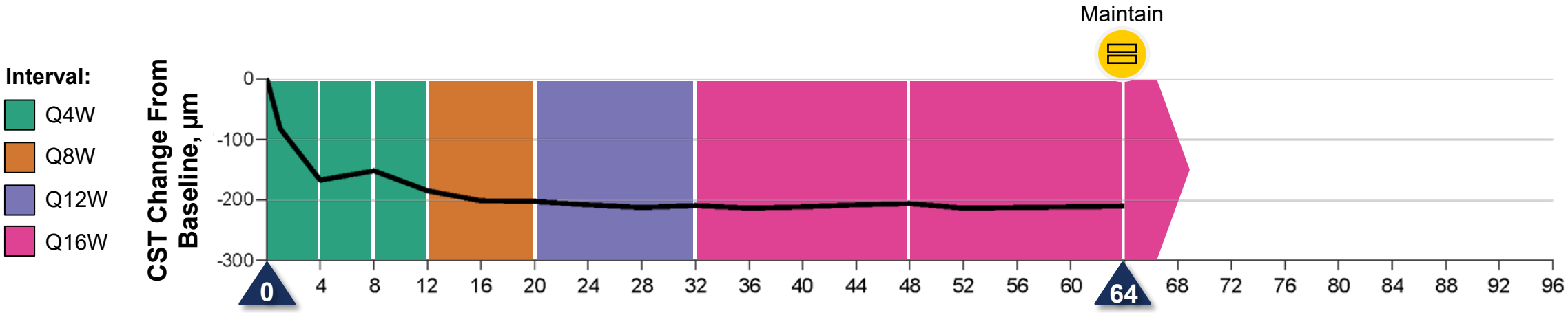


Week 64:
BCVA 83 ETDRS letters
CST 279 µm





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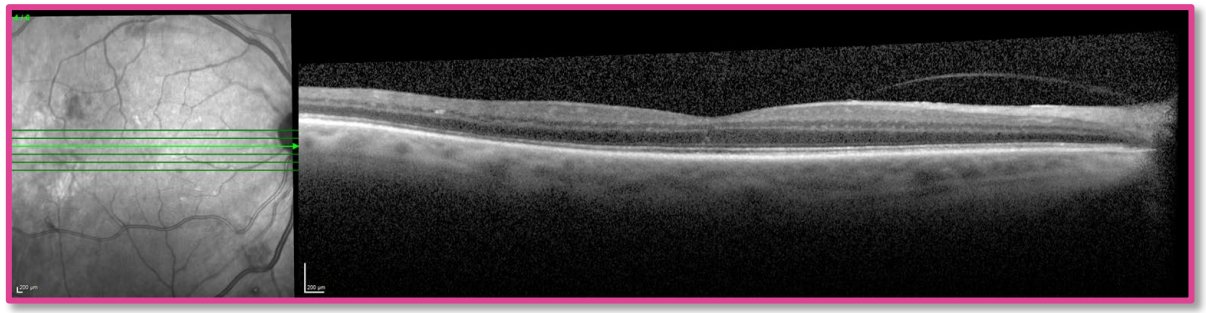
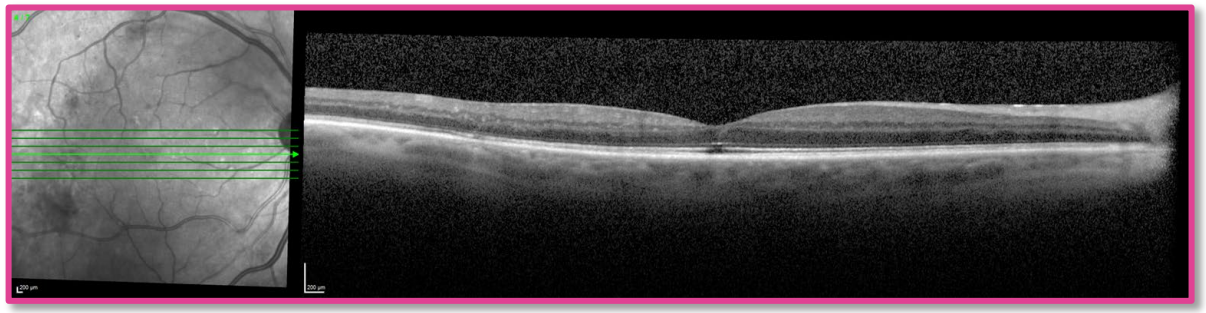
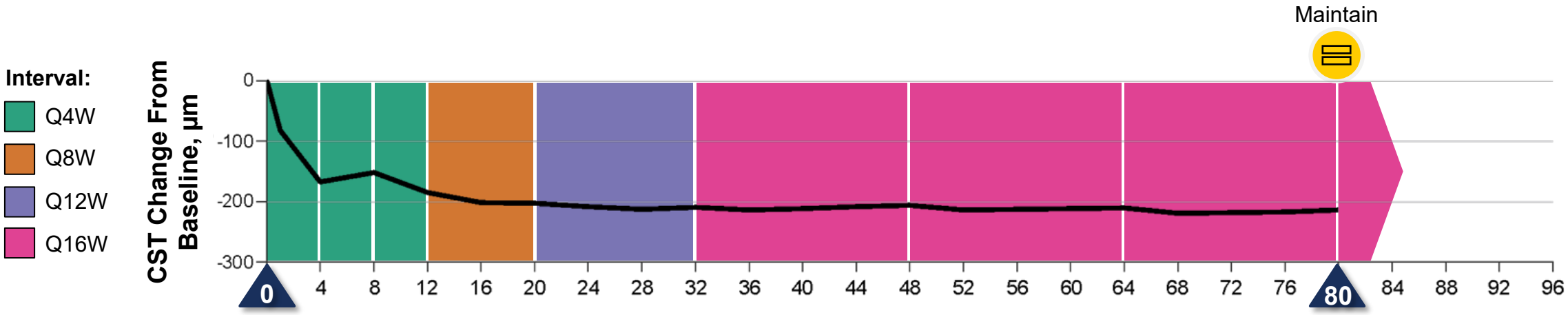


Week 80:
BCVA 81 ETDRS letters
CST 275 µm





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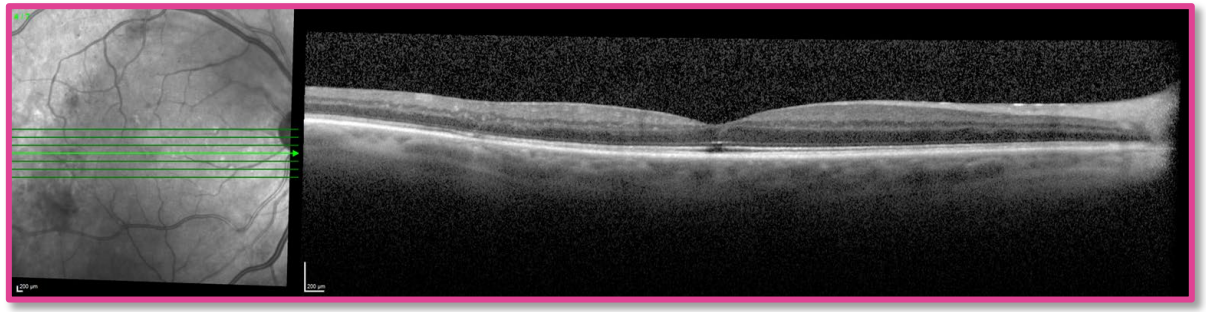

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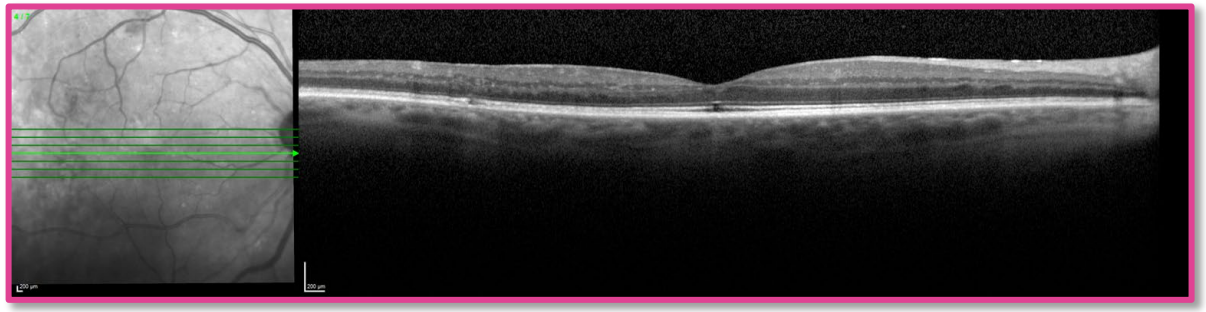

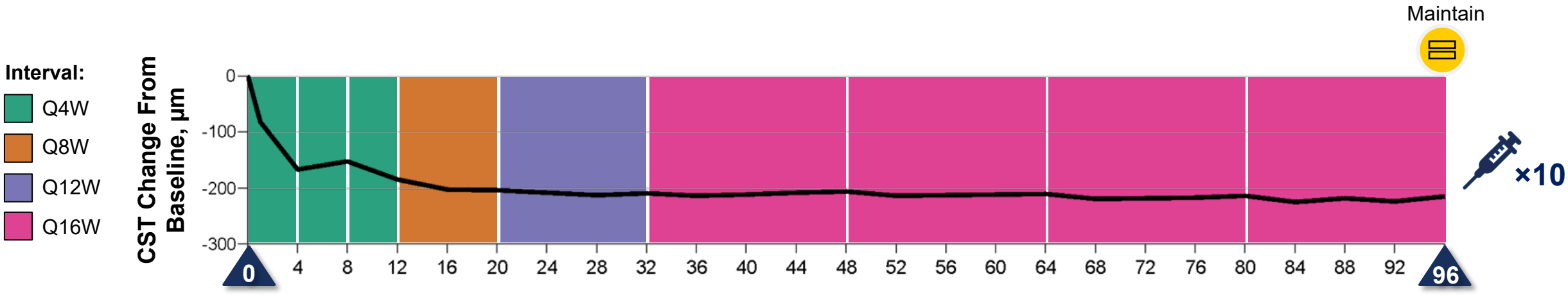

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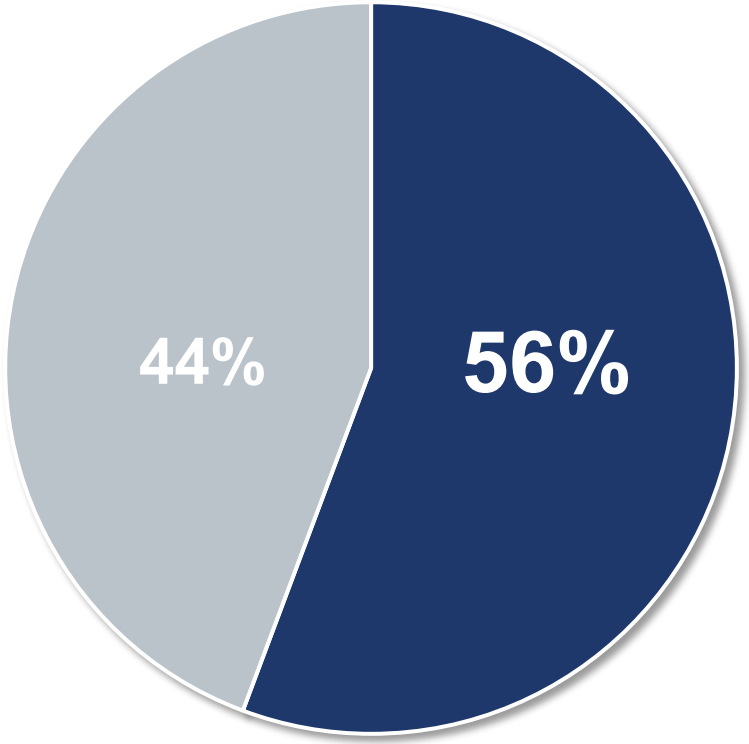
By End of Study, 56% of Faricimab T&E Patients Met Extension Criteria and Could Potentially Have Extended to Q20W

YOSEMITE/RHINE Pooled: Post Hoc Analysis

Faricimab T&E patients
N = 598[a]



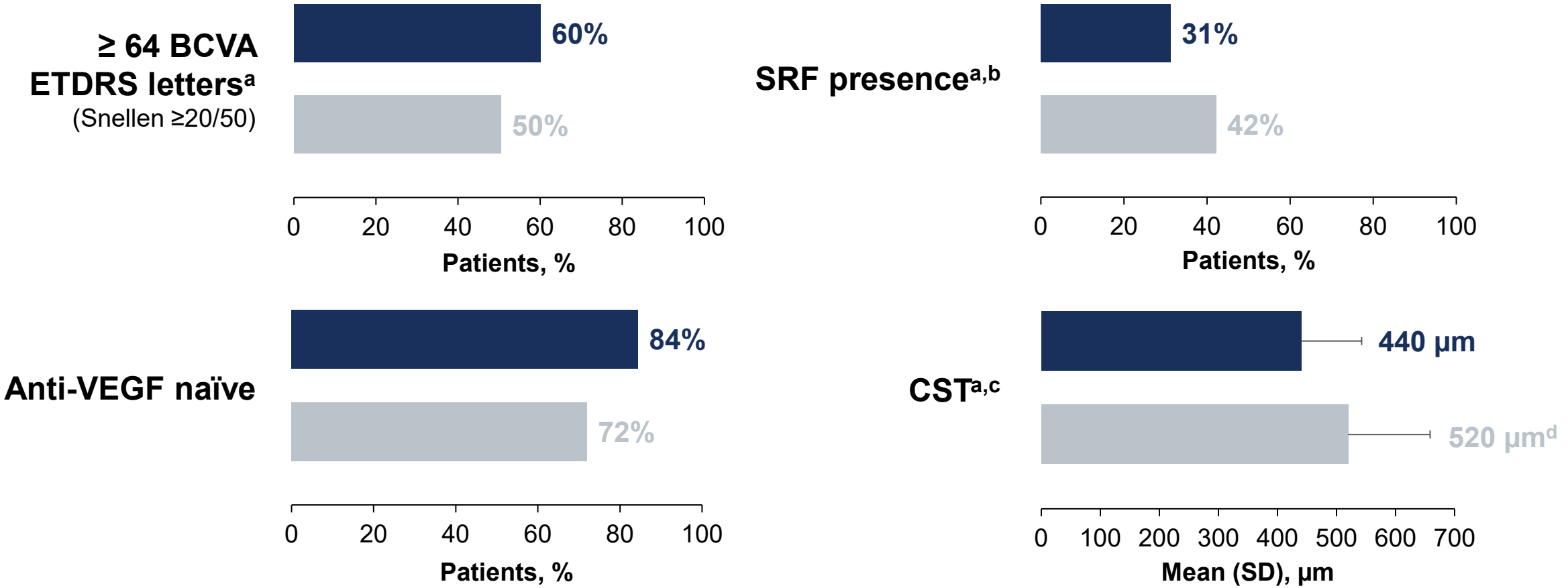
Patients who did not meet criteria for Q20W extension[b]

Patients who completed a Q16W cycle and met criteria for potential Q20W extension[c]

ITT analysis. [a] Includes all patients in the faricimab T&E arm who had not discontinued the study at week 48. [b] Includes all patients in the faricimab T&E arm on ≤ Q16W dosing who did not meet extension criteria.
[c] The same protocol defined extension criteria for personalized T&E was used in this analysis: If the CST value is increased or decreased by ≤ 10% without an associated ≥ 10-letter BCVA decrease.
BCVA, best-corrected visual acuity; CST, central subfield thickness; ITT, intent to treat; Q16W, every 16 weeks; Q20W, every 20 weeks; T&E, treat-and-extend.

Select Baseline Characteristics in Faricimab Patients Who Met vs Did Not Meet Criteria for Potential Q20W Dosing

YOSEMITE/RHINE Pooled: Post Hoc Analysis



[a] In the study eye. [b] Within center 1 mm. [c] ILM-BM. [d] n = 278. [e] Includes all patients in the faricimab T&E arm on ≤ Q16W dosing who met extension criteria. The same protocol defined extension criteria for personalized T&E was used in this analysis: If the CST value is increased or decreased by ≤ 10% without an associated ≥ 10-letter BCVA decrease. [f] Includes all patients in the faricimab T&E arm on ≤ Q16W dosing who did not meet extension criteria.
BCVA, best-corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; ILM-BM, internal limiting membrane to Bruch's membrane; Q16W, every 16 weeks; Q20W, every 20 weeks; SD, standard deviation; SRF, subretinal fluid; T&E, treat-and-extend; VEGF, vascular endothelial growth factor.

Conclusions

Patients on **≥ Q12W** faricimab dosing intervals at week 96 exhibited **stable disease control** with **robust anatomic** and **vision outcomes** through 2 years

56% of faricimab **T&E** patients **met extension criteria** and could **potentially extend to Q20W**

These data support the potential for dual Ang-2/VEGF-A inhibition with faricimab to extend treatment durability with stable disease control for patients with DME

Ang-2, angiopoietin 2; DME, diabetic macular edema; Q12W, every 12 weeks; Q20W, every 20 weeks; T&E, treat-and-extend; VEGF-A, vascular endothelial growth factor A.