Aflibercept 8 mg in Treatment-Naive Macular Edema Secondary to Retinal Vein Occlusion: Primary Results From the QUASAR Study

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Disclosures

- Raman Bhakhri has no disclosures to report
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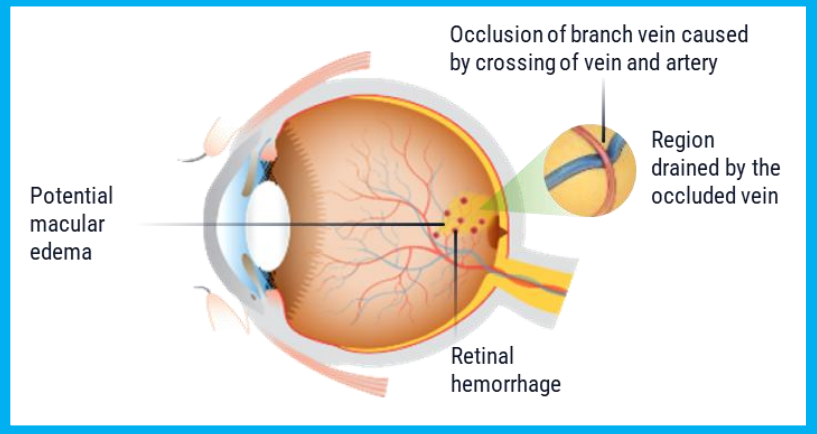
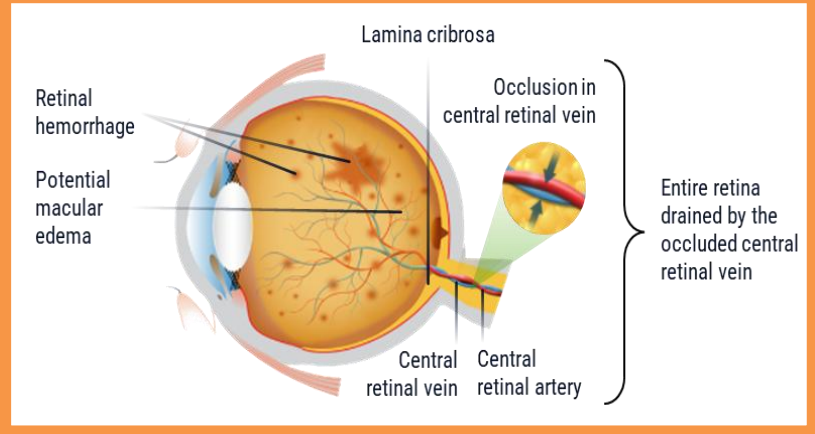
Background

- RVO is the second most common cause of retinal vascular blindness after diabetic retinopathy, affecting approximately 28 million adults worldwide[1]
- BRVO and CRVO are the most common types of RVO[1]
  - HRVO, a less common type of RVO, shares etiologic and clinical characteristics of BRVO and CRVO

BRVO
Blockage of the branch vein
(accounts for ~83.3% of RVO cases[2])



CRVO
Blockage of the central retinal vein
(accounts for ~16.7% of RVO cases[2])

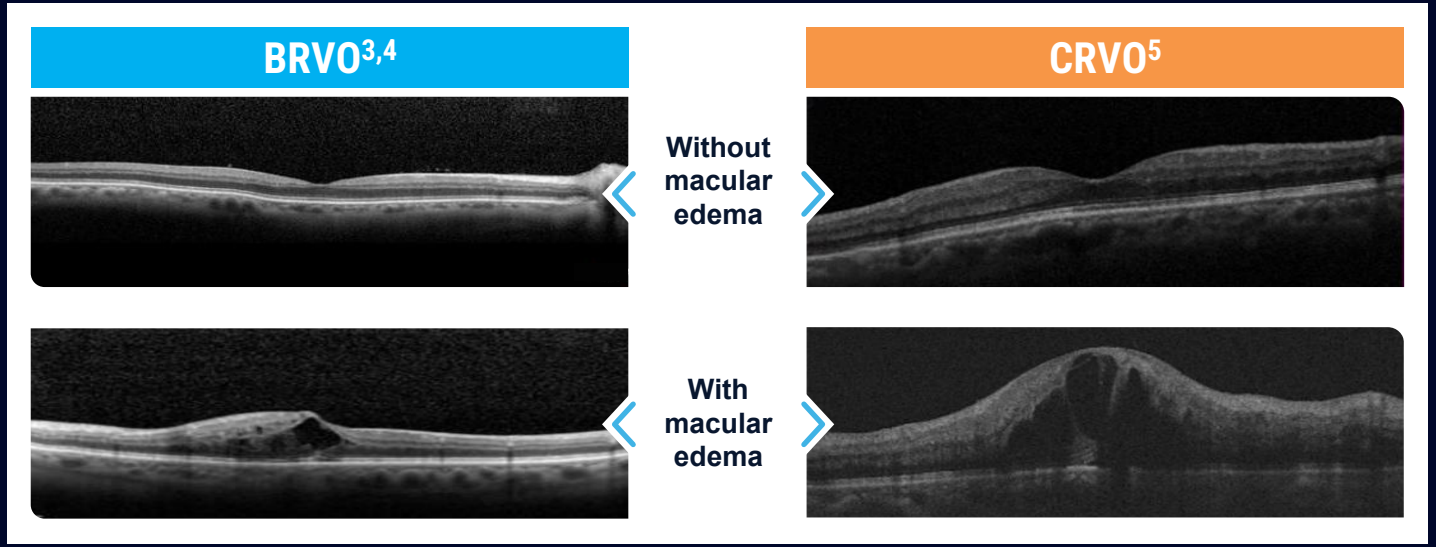


BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; HRVO, hemiretinal vein occlusion; RVO, retinal vein occlusion.

1. Kovach JL et al. *Ophthalmology*. 2025;132:303–343. 2. Song P et al. *J Glob Health*. 2019;9:010427.

Macular Edema Secondary to RVO

- Macular edema is a major complication of RVO that leads to vision loss[1]
- Macular edema secondary to RVO is thought to be caused by fluid flux from vessels to tissue following the expression of VEGF[2]
  - This leads to a breakdown in the blood–retinal barrier and increased vascular permeability[2]



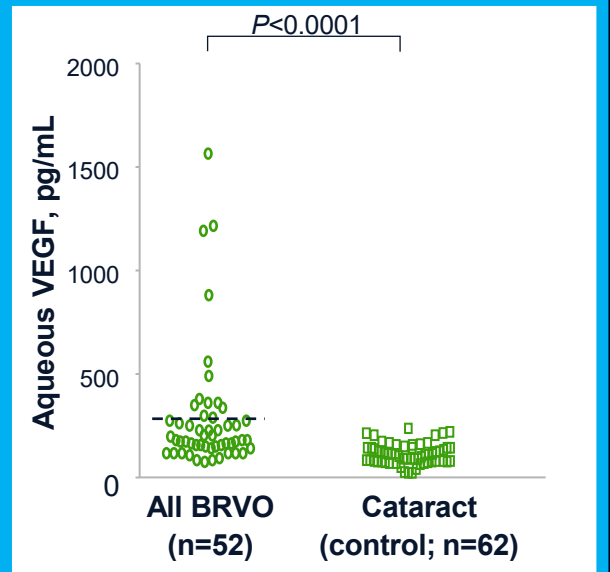
VEGF, vascular endothelial growth factor.

1. Kovach JL et al. *Ophthalmology*. 2025;132:303–343. 2. Li J et al. *J Ophthalmol*. 2017;2017:4936924. 3. Retina Gallery (attributed to Cohen SM). BRVO no macular edema; 2017. Accessed March 10, 2025. https://retinagallery.com/displayimage.php?pid=10219. 4. Retina Gallery (attributed to Cohen SM). BRVO with macular edema; 2014. Accessed March 10, 2025. https://retinagallery.com/displayimage.php?pid=7353. 5. Murakami T et al. *J Clin Med*. 2022;11:4139.

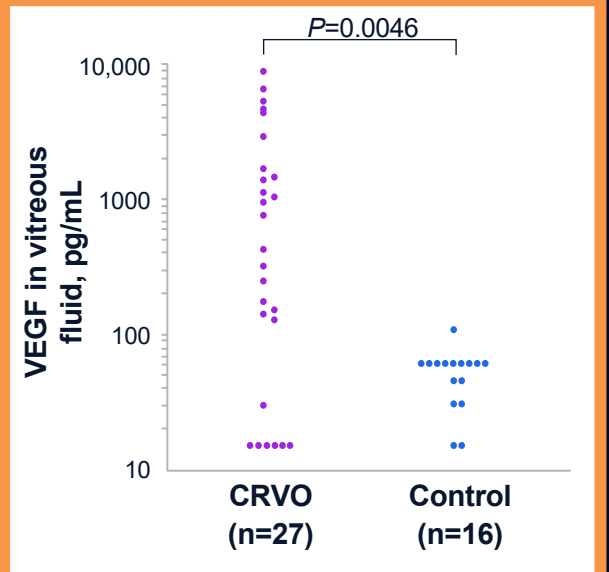
Role of VEGF in RVO

- VEGF is a key pathophysiological driver of retinal vascular diseases, such as nAMD and DME[1,2]
- Overexpression of VEGF is greater in RVO than nAMD and DME[3-5]
- Anti-VEGF therapy is the first-line treatment for BRVO and CRVO[6]
  - Despite robust efficacy and safety of anti-VEGF therapy for RVO in clinical trials, suboptimal outcomes are observed in clinical practice, in part due to the need for more frequent treatment[7]

BRVO[8]



CRVO[9]

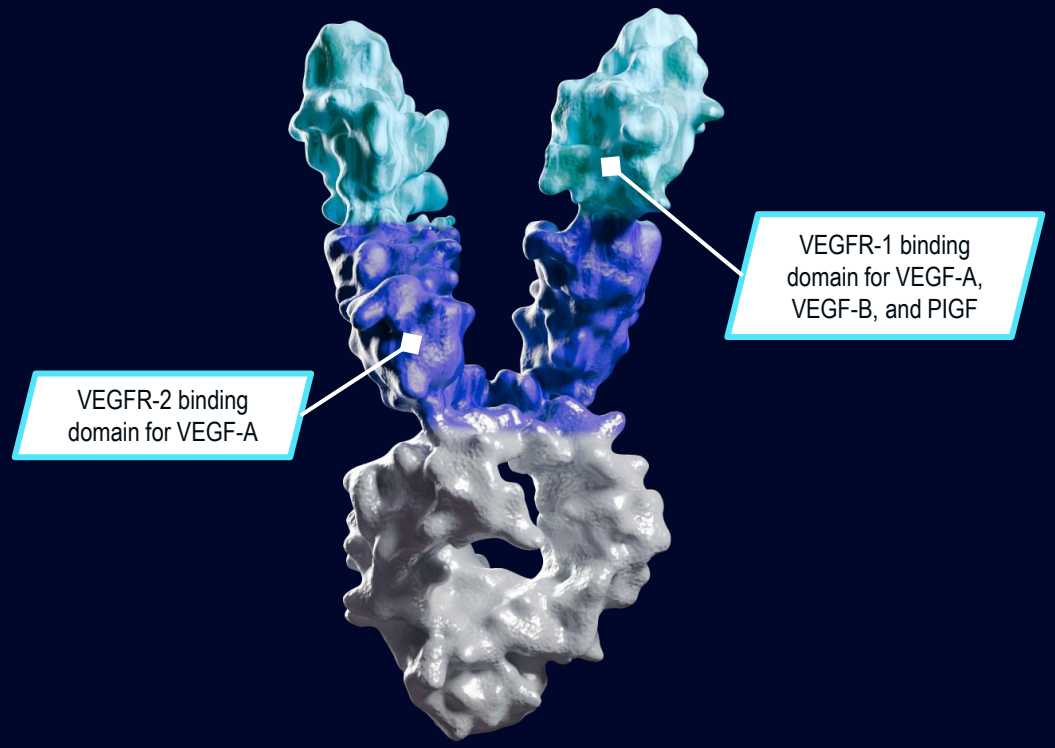


DME, diabetic macular edema; nAMD, neovascular age-related macular degeneration.

1. Uemura A et al. *Prog Retin Eye Res*. 2021;84:100954. 2. Romero-Aroca P et al. *J Diabetes Res*. 2016;2016:2156273. 3. Choi YJ et al. *Invest Ophthalmol Vis Sci*. 2024;65:11. 4. Yi Q-Y et al. *Acta Ophthalmol*. 2020;98:e309–e315. 5. Aiello LP et al. *New Eng J Med*. 1994;331:1480–1487. 6. Kovach JL et al. *Ophthalmology*. 2025;132:303–343. 7. Ciulla T et al. *Br J Ophthalmol*. 2021;105:1696–1704. 8. Fujikawa M et al. *Clin Ophthalmol*. 2013;7:1497–1501. 9. Noma H et al. *Ophthalmology*. 2009;116:87–93.

High-Dose Aflibercept 8 mg

- Aflibercept 8 mg is a novel formulation that delivers a 4-fold higher molar dose than aflibercept 2 mg, potentially suppressing VEGF signaling over a longer duration of time
- Aflibercept 8 mg, with extended dosing intervals of 12 and 16 weeks, has demonstrated comparable efficacy and safety to aflibercept 2 mg in the pivotal PULSAR and PHOTON trials in nAMD and DME, respectively[1,2]
  - Findings from these trials supported regulatory approval of aflibercept 8 mg for the treatment of nAMD, DME, and DR in the United States[3]



The Phase 3 QUASAR study evaluated the efficacy and safety of aflibercept 8 mg versus 2 mg in patients with treatment-naive macular edema following RVO

DR, diabetic retinopathy; PIGF, placental growth factor; VEGFR, vascular endothelial growth factor receptor.

1. Lanzetta P et al. *Lancet*. 2024;403:1141–1152. 2. Brown DM et al. *Lancet*. 2024;403:1153–1163. 3. EYLEA® HD (aflibercept) injection, for intravitreal use. Highlights of prescribing information. Regeneron Pharmaceuticals, Inc.; 2023. Accessed September 14, 2025. https://www.regeneron.com/downloads/eyleahd_fpi.

QUASAR Study Design

Multicenter, randomized, double-masked study in patients with treatment-naive macular edema secondary to RVO
Randomized at BL 1 (2q4) : 1 (8q8/3) : 1 (8q8/5)

2q4
Aflibercept 2 mg every 4 weeks
n=301

8q8/3
Aflibercept 8 mg every 8 weeks after 3 initial monthly injections
n=293

8q8/5
Aflibercept 8 mg every 8 weeks after 5 initial monthly injections
n=298

Primary endpoint at Week 36
Change from BL in BCVA (noninferiority)

Secondary endpoints at Week 36
Number of active injections from BL
Change from BL in CRT

End of study at Week 64

2q4, aflibercept 2 mg administered every 4 weeks; 8q8/3, aflibercept 8 mg administered every 8 weeks after 3 initial monthly injections; 8q8/5, aflibercept 8 mg administered every 8 weeks after 5 initial monthly injections; BL, baseline; BCVA, best-corrected visual acuity; CRT, central retinal thickness.

QUASAR Dosing Regimen

	Day 1	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 28	Wk 32	Wk 36
2q4	X	X	X	X	X	X	X	X	X[b]	T&E
8q8/3	X	X	X	o	X[a]	o	X[a]	o	X[a,b]	T&E
8q8/5	X	X	X	X	X	o	X[a]	o	X[a]	o

☐ Indicates reference visit for DRM assessment (Week 12 for 8q8/3 and Week 20 for 2q4 and 8q8/5)

Primary endpoint: mean change in BCVA (noninferiority)

[a]DRM: Interval Shortening

- Patients in the 8q8/3, 8q8/5, and 2q4 groups could qualify for interval shortening at a dosing visit beginning at Week 16, 24, and 40, respectively
- ***Criteria for interval shortening:***
  - >5-letter loss in BCVA from reference visit[c]

    AND
  - >50-µm increase in CRT from reference visit[c]
- Dosing intervals were shortened by 4-week increments if patients met the DRM criteria and their last dosing interval was ≥Q8

[b]DRM: Interval Extension

- Patients in the 2q4 and 8q8/3 groups could qualify for interval extension at a dosing visit beginning at Week 32 and those in 8q8/5 qualified at Week 40
- ***Criteria for interval extension:***
  - <5-letter loss in BCVA from reference visit[c]

    AND
  - CRT <320 µm on Heidelberg Spectralis (<300 µm on Cirrus or Topcon SD-OCT)
- Dosing intervals were extended by 4-week increments if DRM criteria were met

Stippled boxes = initial treatment phase; X = active injection; o = sham injections. Figure does not reflect all dosing options if the intervals are shortened.
[c]Reference visit defined as Week 12 for 8q8/3, and Week 20 for 8q8/5 and 2q4.
DRM, dose regimen modification; Q8, every 8 weeks; SD-OCT, spectral domain-optical coherence tomography; T&E, treat and extend; Wk, week.

Key Eligibility Criteria

Inclusion Criteria

- Adults (aged ≥18 years) with treatment-naive macular edema secondary to RVO (BRVO, CRVO, or HRVO) diagnosed within 16 weeks of the screening visit
- BCVA of 73 to 24 ETDRS letters (Snellen equivalent 20/40 to 20/320)
- Decrease in BCVA determined to be primarily the result of RVO
- Mean CRT ≥320 μm on Heidelberg Spectralis or ≥300 μm on Cirrus or Topcon SD-OCT, as confirmed by the reading center

Exclusion Criteria

- Concurrent disease that causes substantial decrease in BCVA, is expected to limit BCVA recovery, or is likely to require medical or surgical intervention in the study eye during the study
- Advanced nAMD or geographic atrophy, DME, and DR
- Uncontrolled glaucoma (IOP >25 mmHg despite antiglaucoma medication) in the study eye

ETDRS, Early Treatment Diabetic Retinopathy Study; IOP, intraocular pressure.

QUASAR Study Sites

QUASAR is a **global** study conducted at 237 sites in 27 countries

Patient Disposition at Week 36

	2q4	8q8/3	8q8/5	Total
Randomized, n	302	294	298	894
Treated, n (%)	301 (99.7)	293 (99.7)	298 (100)	892 (99.8)
Completing Week 36, n (%)	287 (95.0)	278 (94.6)	273 (91.6)	838 (93.7)
Discontinued before Week 36, n (%)	14 (4.6)	15 (5.1)	25 (8.4)	54 (6.0)
Reasons for discontinuation, n (%)				
Withdrawal by patient	8 (2.6)	8 (2.7)	16 (5.4)	32 (3.6)
Adverse events	2 (0.7)	0	2 (0.7)	4 (0.4)
Death	2 (0.7)	2 (0.7)	3 (1.0)	7 (0.8)
Lost to follow-up	2 (0.7)	3 (1.0)	3 (1.0)	8 (0.9)
Other[a]	0	2 (0.7)	1 (0.3)	3 (0.3)

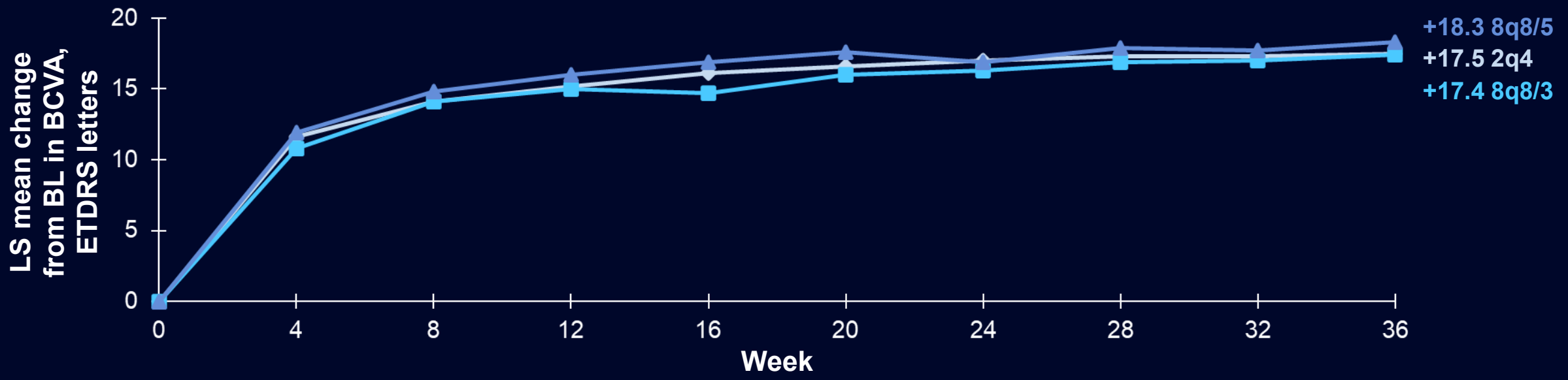
[a]Includes “logistical problem,” “physician decision,” and “protocol deviation.” Categories were combined to maintain masking of individual patients.

Baseline Demographics and Disease Characteristics

	2q4 (n=301)	8q8/3 (n=293)	8q8/5 (n=298)	Total (n=892)
Age, years	65.9 (11.7)	65.8 (11.5)	65.8 (11.5)	65.9 (11.6)
Female, n (%)	144 (47.8)	136 (46.4)	146 (49.0)	426 (47.8)
Race, n (%)				
Asian	101 (33.6)	91 (31.1)	97 (32.6)	289 (32.4)
Black or African American	8 (2.7)	7 (2.4)	9 (3.0)	24 (2.7)
White	178 (59.1)	173 (59.0)	177 (59.4)	528 (59.2)
Other[a]	1 (0.3)	0	4 (1.3)	5 (0.6)
Not reported	13 (4.3)	22 (7.5)	11 (3.7)	46 (5.2)
Hispanic or Latino, n (%)	22 (7.3)	25 (8.5)	14 (4.7)	61 (6.8)
History of hypertension, n (%)	187 (62.1)	192 (65.5)	196 (65.8)	575 (64.5)
RVO type, n (%)[b]				
BRVO	149 (49.5)	159 (54.3)	159 (53.4)	467 (52.4)
CRVO	117 (38.9)	99 (33.8)	102 (34.2)	318 (35.7)
HRVO	35 (11.6)	35 (11.9)	37 (12.4)	107 (12.0)
BCVA, ETDRS letters	54.1 (14.3)	55.2 (13.6)	55.4 (13.4)	54.9 (13.8)
CRT, µm[c]	651 (240)	626 (230)	609 (213)	629 (229)

FAS. Data are mean (SD) unless otherwise indicated.
[a]Includes American Indian or Alaskan native, native Hawaiian or other Pacific Islander, and Multiple. [b]Assessed by the reading center. [c]BL CRT measurement was missing for 1 patient in the 2q4 group. FAS, full analysis set.

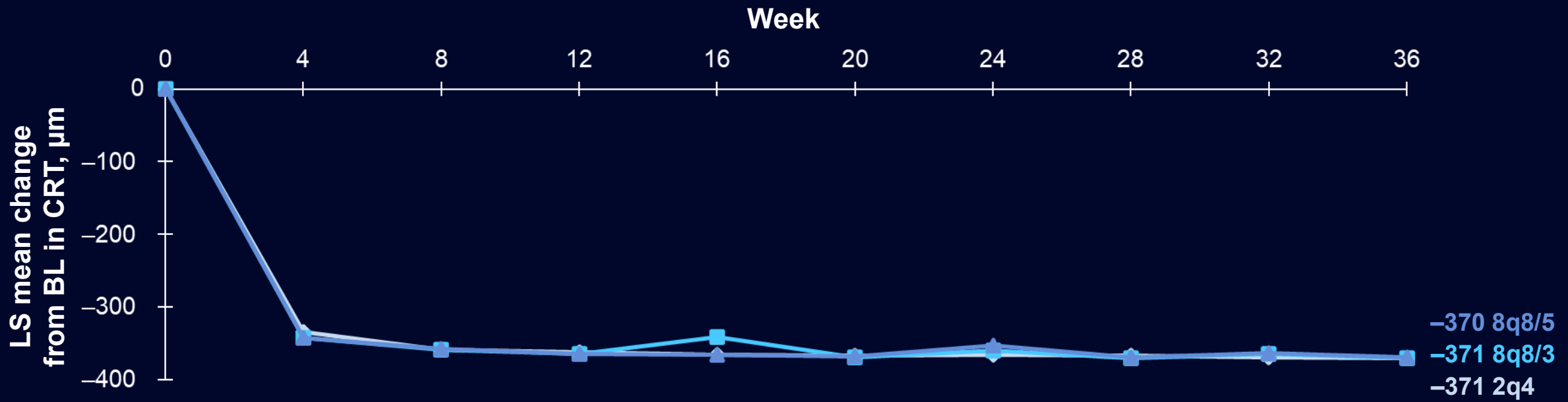
Both Aflibercept 8-mg Groups Achieved Noninferior BCVA Gains Compared to 2q4 at Week 36 With Fewer Injections



	Absolute mean BCVA at Week 36[a]	LS mean change from BL at Week 36	Difference in LS means vs 2q4	2-sided 95% CI	1-sided test for noninferiority at 4-letter margin	Mean number of injections through Week 36[b]
2q4 (n=301)	72.0	17.5				8.8
8q8/3 (n=293)	72.8	17.4	–0.1	–2.0, 1.9	*P*<0.0001	6.1
8q8/5 (n=298)	74.6	18.3	0.8	–1.1, 2.7	*P*<0.0001	6.9

FAS. LS means were generated using a mixed model for repeated measures with BL BCVA as a covariate; treatment group (8q8/3, 8q8/5, 2q4), visit, and stratification variables (geographic region [Japan vs Asian-Pacific vs Europe vs America], BL BCVA [<60 vs ≥60 letters], RVO type [CRVO/HRVO vs BRVO]) as fixed factors; and terms for the interaction between BL BCVA and visit and treatment and visit. [a]Observed values (censoring data post-ICE). [b]FAS, patients who completed Week 36 visit.
CI, confidence interval; ICE, intercurrent event; LS, least squares.

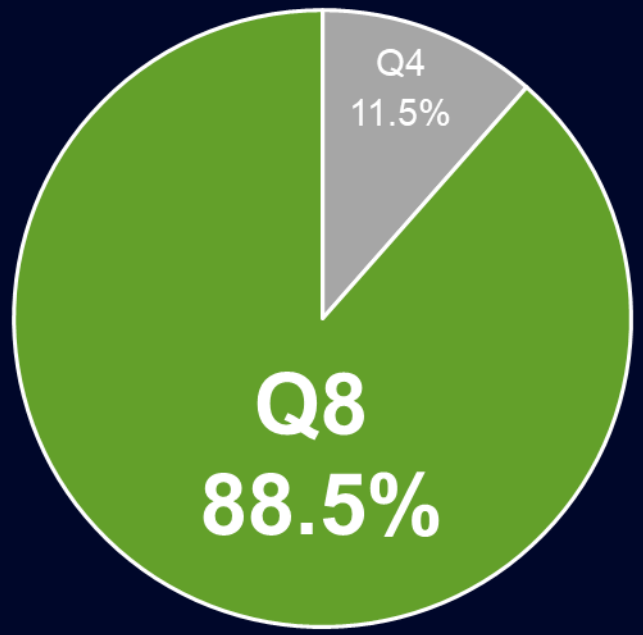
Both Aflibercept 8-mg Groups Achieved Robust CRT Reductions Compared to 2q4 at Week 36 With Fewer Injections



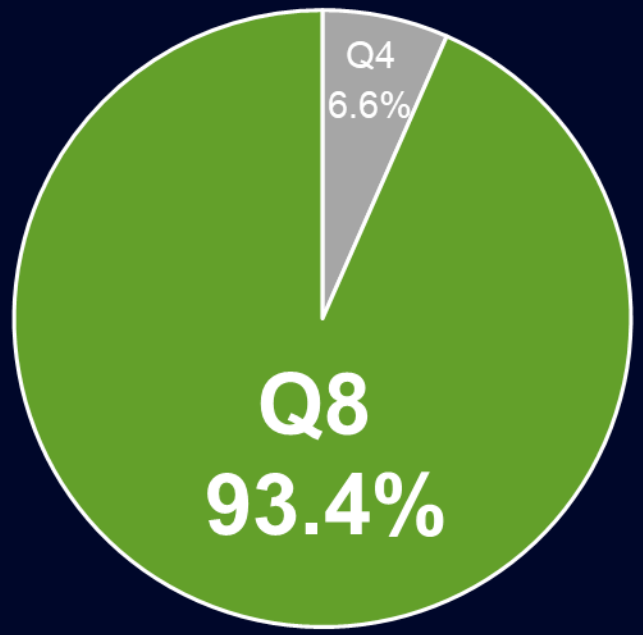
	Absolute mean CRT at BL (µm)	Absolute mean CRT at Week 36 (µm)[a]	LS mean change from BL at Week 36	Mean number of injections through Week 36[b]
2q4 (n=301)	651	257	–371	8.8
8q8/3 (n=293)	626	258	–371	6.1
8q8/5 (n=298)	609	259	–370	6.9

FAS. LS means were generated using a mixed model for repeated measures with BL CRT as a covariate; treatment group (8q8/3, 8q8/5, 2q4), visit, and stratification variables (geographic region [Japan vs Asian-Pacific vs Europe vs America], BL BCVA [<60 vs ≥60 letters], RVO type [CRVO/HRVO vs BRVO]) as fixed factors; and terms for the interaction between BL CRT and visit and treatment and visit. [a]Observed values (censoring data post-ICE). [b]FAS, patients who completed Week 36 visit.

Majority of Aflibercept 8-mg Patients Maintained Q8 Dosing Through Week 36



8q8/3
(n=278)

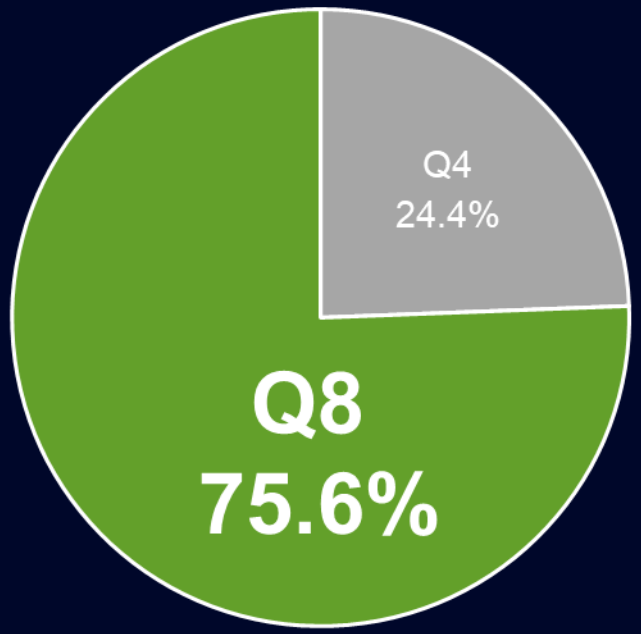


8q8/5
(n=273)

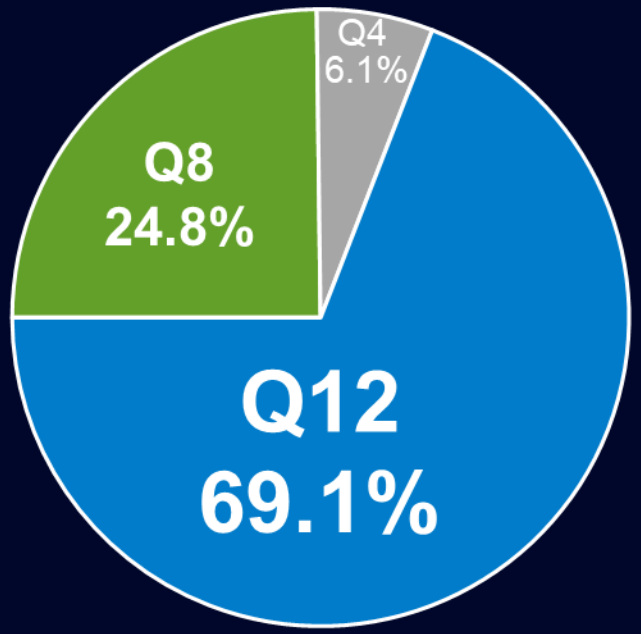
In total, 88.5% in the 8q8/3 group and 93.4% in the 8q8/5 group maintained Q8 dosing as per the treatment arm regimen without the need for interval shortening

FAS, patients who completed Week 36. Patients in the aflibercept 8-mg groups with a >5-letter loss in vision and a >50-µm increase in CRT compared with reference visit (Week 12 for 8q8/3 and Week 20 for 8q8/5) had their dosing interval shortened to Q4.
Q4, every 4 weeks; Q8, every 8 weeks.

Last Assigned Dosing Interval at Week 36 for Patients Eligible for Interval Extension



2q4
(n=287)

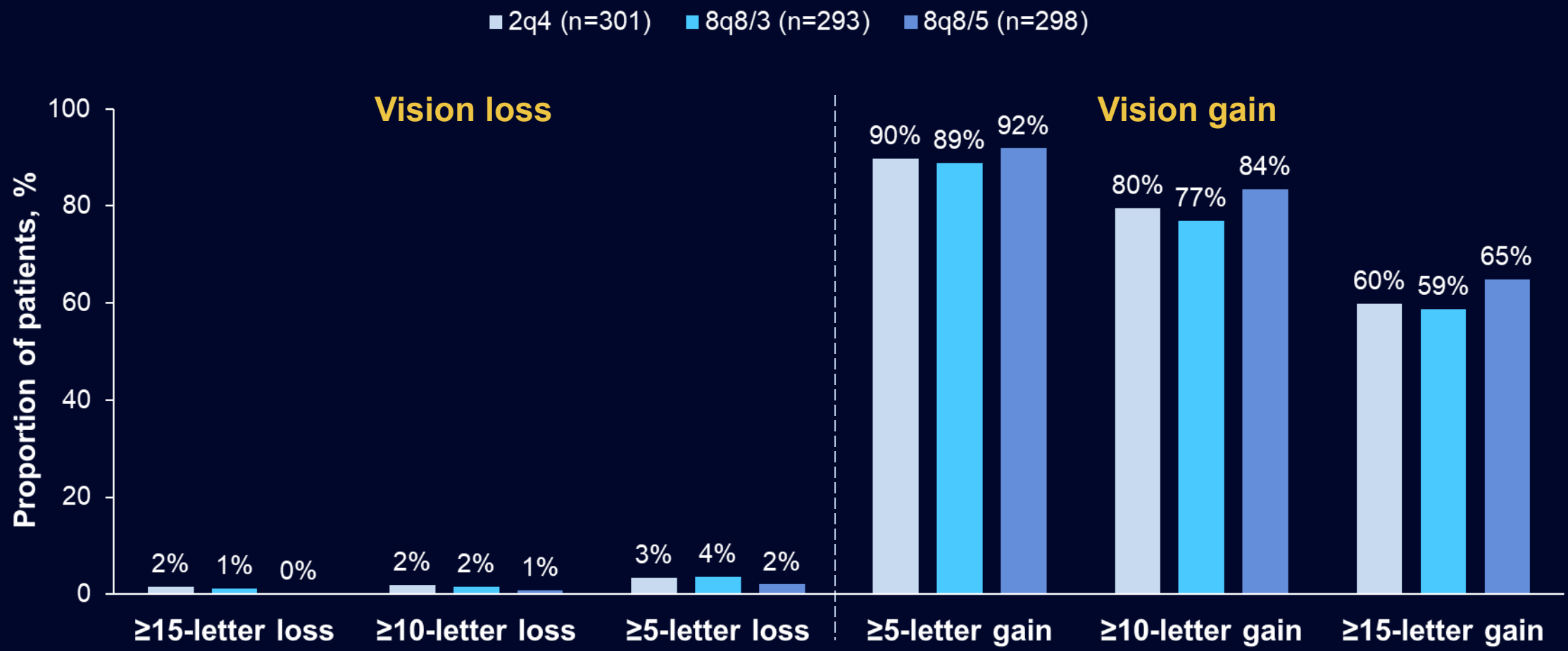


8q8/3
(n=278)

Per study design, dosing interval extension was not possible in the 8q8/5 group until Week 40

FAS, patients who completed Week 36.
Q12, every 12 weeks.

Proportion of Patients With ≥5-, 10-, or 15-Letter Loss or Gain at Week 36



FAS, observed values (censoring data post-ICE).

Ocular and Nonocular Safety Through Week 36

	2q4 (n=301)	8q8/3 (n=293)	8q8/5 (n=298)	All 8 mg (n=591)
Ocular TEAEs, n (%)	98 (32.6)	117 (39.9)	97 (32.6)	214 (36.2)
Ocular SAEs, n (%)	8 (2.7)	4 (1.4)	4 (1.3)	8 (1.4)
Intraocular inflammation, n (%)	4 (1.3)	2 (0.7)	1 (0.3)	3 (0.5)
Anterior chamber cell	1 (0.3)	0	0	0
Eye inflammation	1 (0.3)	0	0	0
Iritis	0	1 (0.3)	0	1 (0.2)
Uveitis	0	0	1 (0.3)	1 (0.2)
Endophthalmitis	2 (0.7)	1 (0.3)	0	1 (0.2)
Nonocular SAEs, n (%)	26 (8.6)	22 (7.5)	28 (9.4)	50 (8.5)
APTC events, n (%)	5 (1.7)	0	3 (1.0)	3 (0.5)
Deaths, n (%)	2 (0.7)	2 (0.7)	3 (1.0)	5 (0.8)

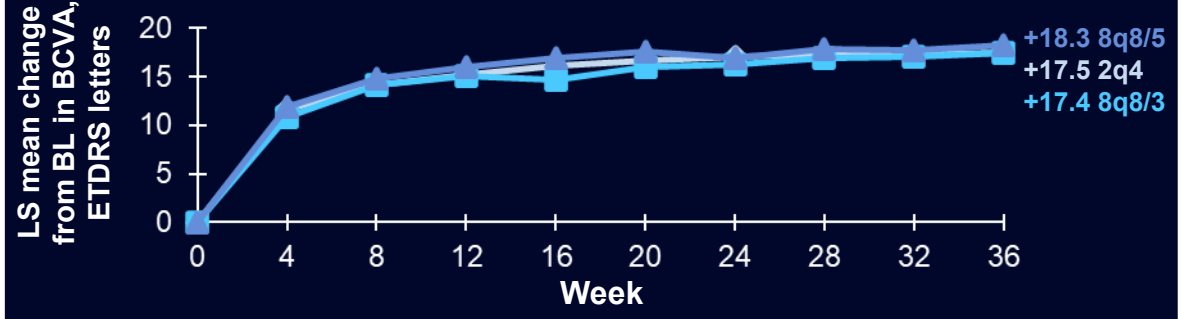
- No cases of occlusive retinal vasculitis were reported
- The safety profile of aflibercept 8 mg was consistent with the established safety of aflibercept 2 mg

Safety analysis set. Ocular TEAE and SAE data are presented for the study eye.
APTC, Anti-Platelet Trialists' Collaboration; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Conclusions

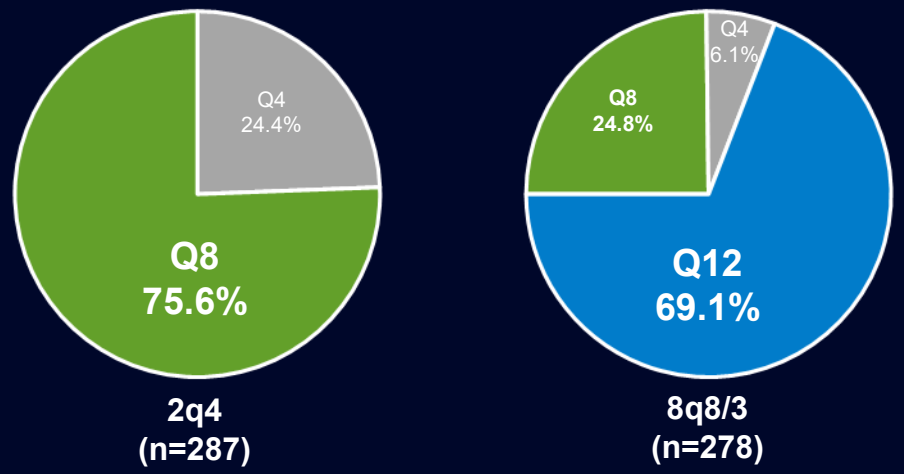
- Aflibercept 8q8/3 and 8q8/5 achieved **noninferior BCVA gains and robust reductions in CRT with fewer injections** compared with 2q4 at Week 36
- The vast majority of patients in the aflibercept 8-mg groups **maintained ≥Q8 dosing** through Week 36 without interval shortening
- The safety profile of aflibercept 8 mg in patients with macular edema secondary to RVO was **consistent with the established safety of aflibercept 2 mg and 8 mg**

Mean Change in BCVA Through Week 36[a]



	Absolute mean BCVA at Week 36[b]	LS mean change from BL at Week 36	Difference in LS means vs 2q4	2-sided 95% CI	1-sided test for noninferiority at 4-letter margin	Mean number of injections through Week 36[c]
2q4 (n=301)	72.0	17.5				**8.8**
8q8/3 (n=293)	72.8	17.4	–0.1	–2.0, 1.9	*P*<0.0001	6.1
8q8/5 (n=298)	74.6	18.3	0.8	–1.1, 2.7	*P*<0.0001	6.9

Last Assigned Dosing Interval at Week 36 for Patients Eligible for Interval Extension[c]



[a]FAS. LS means were generated using a mixed model for repeated measures with BL BCVA as a covariate; treatment group (8q8/3, 8q8/5, 2q4), visit, and stratification variables (geographic region [Japan vs Asian-Pacific vs Europe vs America], BL BCVA [<60 vs ≥60 letters], RVO type [CRVO/HRVO vs BRVO]) as fixed factors; and terms for the interaction between BL BCVA and visit and treatment and visit. [b]Observed values (censoring data post-ICE). [c]FAS, patients who completed Week 36.