Aflibercept 8 mg in Retinal Vein Occlusion: Primary Endpoint Results from the QUASAR study

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Disclosures

- **Richard Gale** is a consultant for AbbVie, Allergan, Apellis, Astellas, Bayer, Biogen, Boehringer Ingelheim, Novartis, Ocular Therapeutix, Roche, and Santen, and conducts research for Bayer, Novartis, and Roche
- The ongoing QUASAR trial (NCT05850520) is sponsored by Bayer AG (Leverkusen, Germany). The sponsor participated in the design and conduct of the study, analysis of the data, and preparation of this abstract
- This study includes research conducted on human patients. Institutional Review Board/Institutional Ethics Committee approval was obtained prior to study initiation
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- The QUASAR group wish to thank all patients and investigators of the QUASAR trial

QUASAR Study Design

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

2q4
Aflibercept 2 mg every 4 weeks[a]
n=301

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

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

Primary endpoint at Week 36
Change from baseline in BCVA (non-inferiority)

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

End of study at Week 64

Full analysis set/safety analysis set. [a]With opportunity for extension per DRM as explained on the next slide.
BCVA, best-corrected visual acuity; **CRT**, central subfield retinal thickness; **DRM**, dose regimen modification; **RVO**, retinal vein occlusion; **2q4**: Aflibercept 2 mg administered every 4 weeks; **8q8/3**: Aflibercept 8 mg administered every 8 weeks, after 3 initial injections at 4-week intervals; **8q8/5**: Aflibercept 8 mg administered every 8 weeks, after 5 initial injections at 4-week intervals.

QUASAR: Dosing Schedule Regimen Modification Through Week 36

	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	T&E
8q8/3	X	X	X	o	X	o[a]	X	o[b]	X	T&E
8q8/5	X	X	X	X	X	o	X	o[b]	X	o[c]

DRM for Interval Shortening

Dosing interval shortened by 4 weeks if the last dosing interval was >4 weeks and below criteria are met at a dosing visit:

- BCVA loss >5 letters from reference visit, AND
- >50 µm increase in CRT from reference visit*

*Reference is Week 12 for 8q8/3 and Week 20 for 8q8/5 and 2q4

DRM for Interval Extension

Dosing interval extended by 4 weeks starting at Week 32 for 8q8/3 and 2q4 and at Week 40 for 8q8/5 if both the following criteria are met at a dosing visit:

- BCVA loss <5 letters from reference visit*, AND
- CRT <320 µm Heidelberg/<300 µm Cirrus or Topcon SD-OCT

*Reference is Week 12 for 8q8/3 and Week 20 for 8q8/5 and 2q4

Stippled boxes = initial treatment phase; X = active injection; o = sham injections. Note: Table does not reflect all dosing options once a patient's dosing interval is shortened.
[a]Active injection for participants meeting DRM criteria at Week 16. [b]Active injection for participants meeting DRM criteria at Week 16 or 24. [c]Active injection for participants meeting DRM at Weeks 16, 24, or 32. **SD-OCT**, spectral domain-optical coherence tomography; **T&E**, treat and extend; **Wk**, week.

Key Inclusion/Exclusion Criteria

Inclusion Criteria

- Adults ≥18 years of age with treatment naïve macular edema secondary to RVO (BRVO, CRVO, or HRVO) diagnosed within 16 weeks of screening visit
- ETDRS BCVA letter score of 73 to 24 (Snellen equivalent 20/40 to 20/320)
- Decrease in BCVA determined to be primarily the result of RVO
- Mean CRT ≥300 µm on Cirrus or Topcon SD-OCT or ≥320 µm on Heidelberg Spectralis, 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 during the study in the study eye
- Advanced nAMD or geographic atrophy, diabetic macular edema, and diabetic retinopathy
- Uncontrolled glaucoma (IOP >25 mmHg despite anti-glaucoma medication) in the study eye
- Intraocular inflammation or infection within 12 weeks of screening in either eye at screening
- Extraocular/periocular inflammation or infection in either eye at screening
- Uncontrolled blood pressure (SBP >160 mmHg or DBP >95 mmHg) or diabetes mellitus at screening
- History of cerebrovascular accident or myocardial infarction within 24 weeks of screening

BRVO, branch retinal vein occlusion; **CRVO**, central retinal vein occlusion; **DBP**, diastolic blood pressure; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **HRVO**, hemiretinal vein occlusion; **IOP**, intraocular pressure; **nAMD**, neovascular age-related macular degeneration; **SBP**, systolic blood pressure.

QUASAR Study Sites

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

Patient Disposition at Week 36

	2q4	8q8/3	8q8/5	Total
Randomized, n	302	294	298	894
Treated	301 (99.7)	293 (99.7)	298 (100)	892 (99.8)
Completing Week 36	287 (95.0)	278 (94.6)	273 (91.6)	838 (93.7)
Discontinued before Week 36	14 (4.6)	15 (5.1)	25 (8.4)	54 (6.0)
Reasons for discontinuation				
Withdrawal by subject	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)

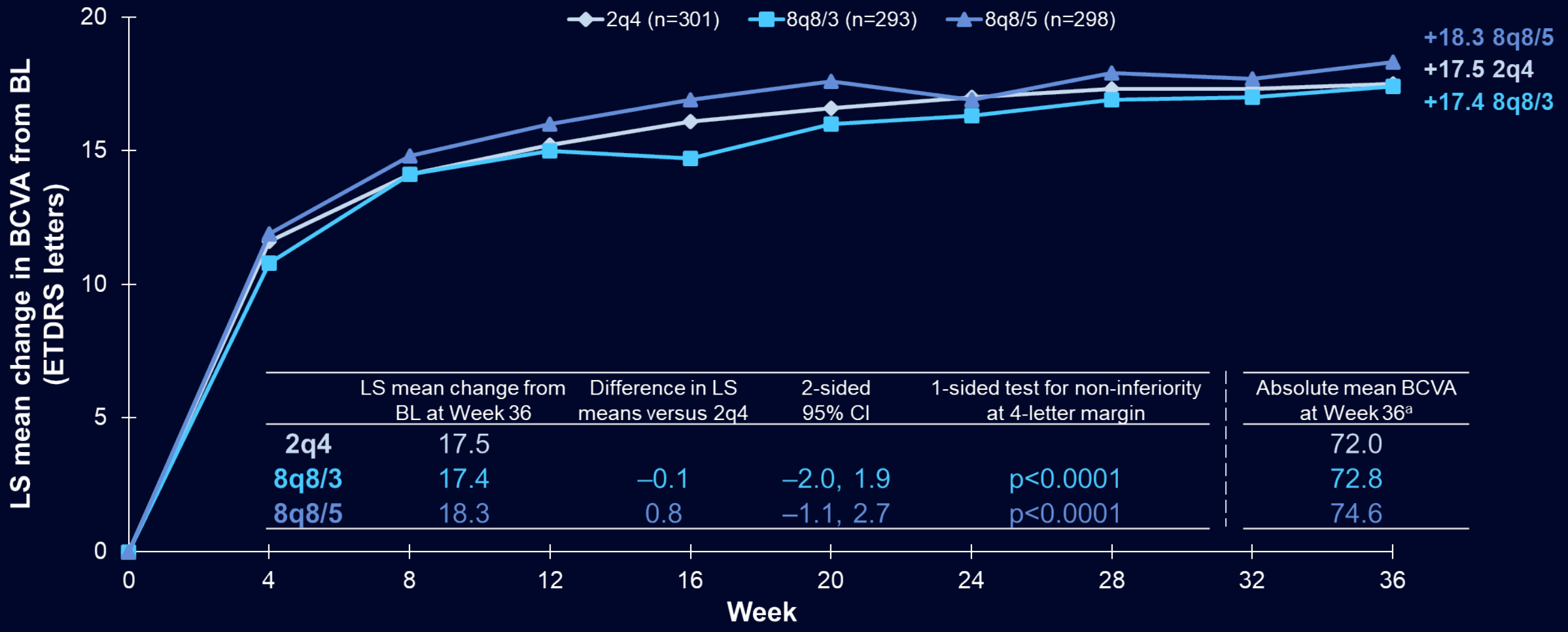
Data are n (%) unless otherwise indicated. [a]Includes "logistical problem", "physician decision", and "protocol deviation". Categories were combined to maintain masking of individual patients.

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)
Medical 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)

Full analysis set. Data are mean (SD) unless otherwise indicated. [a]Includes American Indian or Alaskan native, native Hawaiian or other Pacific Islander, and Multiple. [b]Reading center assessed [c]2q4, n=300; Total, n=891. **SD,** standard deviation.

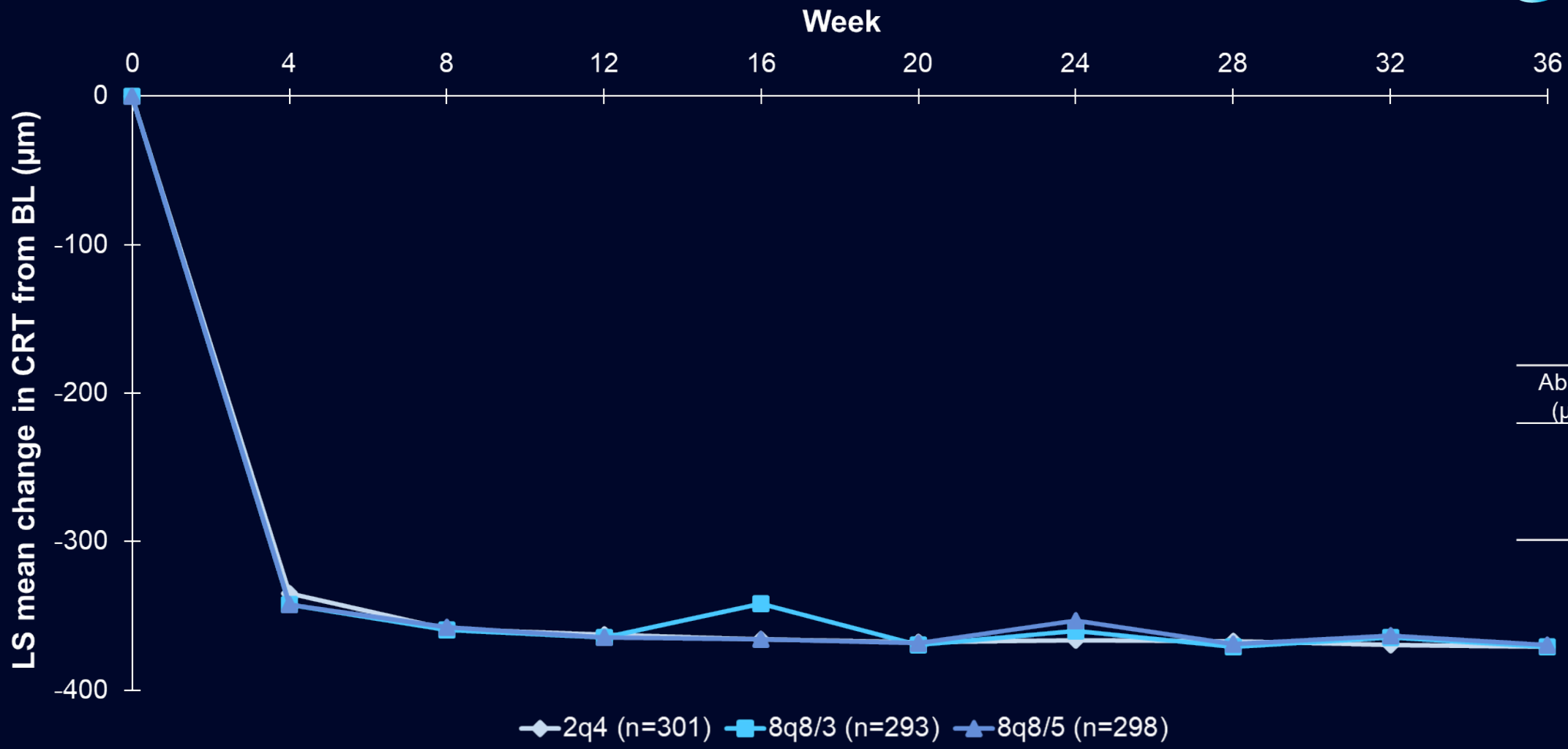
Primary Endpoint Met: Non-inferior BCVA Gains for Both 8q8 Groups Compared with 2q4



	LS mean change from BL at Week 36	Difference in LS means versus 2q4	2-sided 95% CI	1-sided test for non-inferiority at 4-letter margin	Absolute mean BCVA at Week 36[a]
2q4	17.5				72.0
8q8/3	17.4	–0.1	–2.0, 1.9	p<0.0001	72.8
8q8/5	18.3	0.8	–1.1, 2.7	p<0.0001	74.6

Full analysis set. LS means were generated using a mixed model for repeated measures with baseline BCVA as a covariate; treatment group (aflibercept 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 baseline BCVA and visit and treatment and visit. [a]Observed values (censoring data post-ICE). **BL**, baseline; **CI**, confidence interval; **ICE**, intercurrent event; **LS**, least squares.

Early, Robust Reductions in CRT Maintained Through Week 36

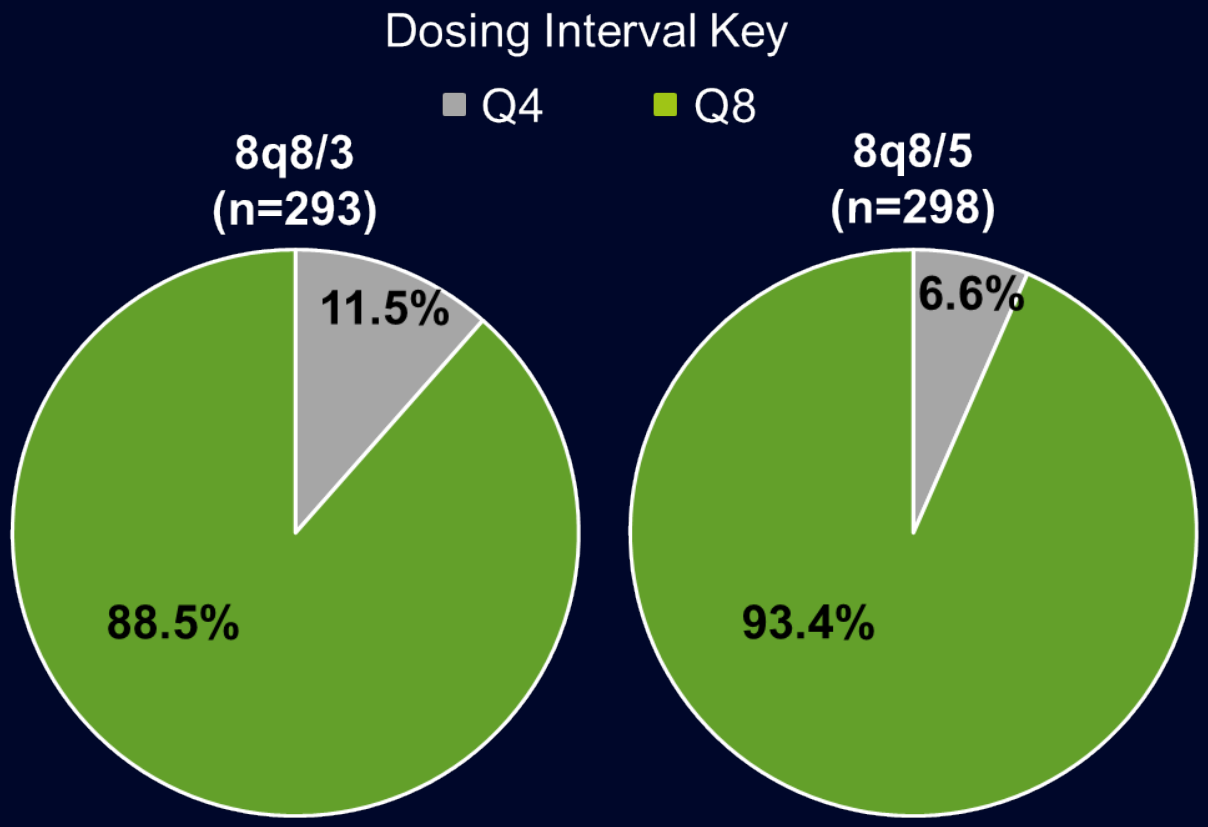


Absolute mean CRT (µm) at Week 36[a]
257
258
259

–370 8q8/5
–371 8q8/3
–371 2q4

Full analysis set. LS means were generated using a mixed model for repeated measures with baseline CRT as a covariate; treatment group (aflibercept 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 baseline CRT and visit and treatment and visit. [a]Observed values (censoring data post-ICE).

Most Patients in 8q8 Groups Maintained Q8 Dosing Interval Through Week 36



88.5% in the 8q8/3 group 93.4% in the 8q8/5 group maintained an Q8 dosing interval

DRM criteria

Dosing interval **shortened** by 4 weeks if last dosing interval was >4 weeks and the below criteria are met at a dosing visit:

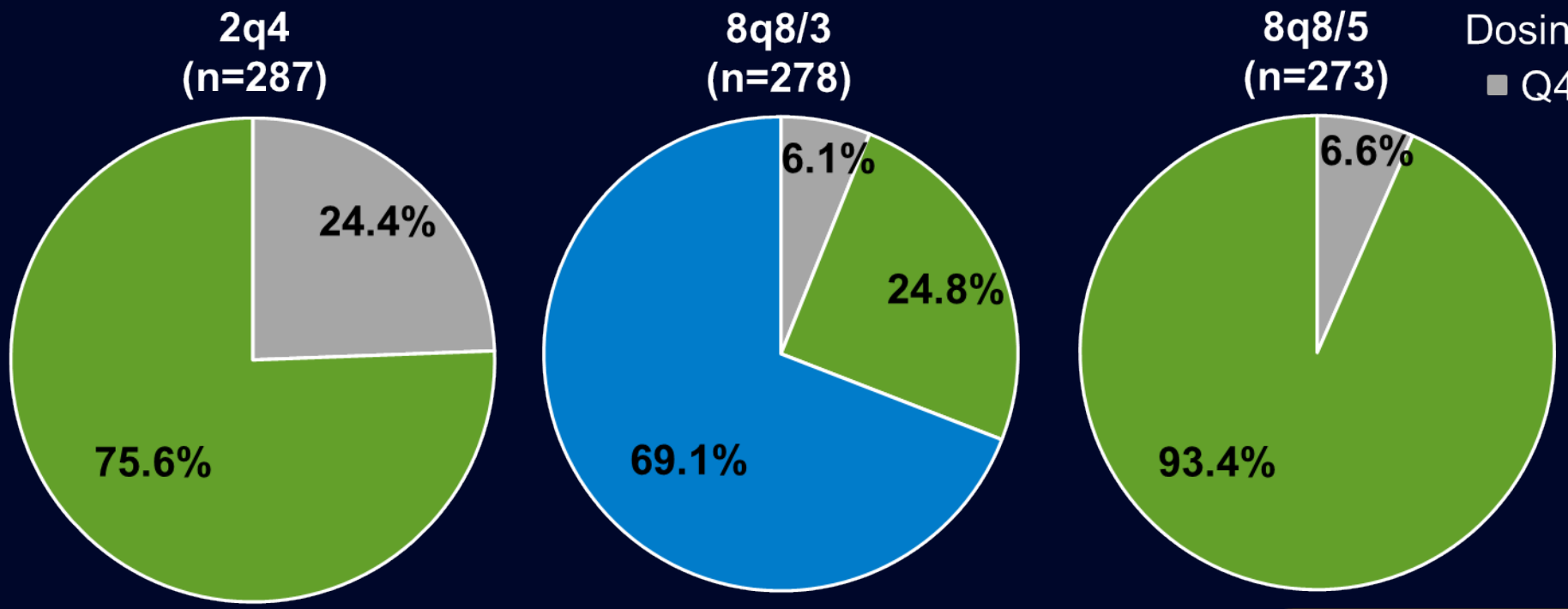
- BCVA loss >5 letters from reference visit, AND
- >50 µm increase in CRT from reference visit

Dosing interval **extended** by 4 weeks starting at Week 32 for 8q8/3 and 2q4 and at Week 40 for 8q8/5 if both the following criteria are met at a dosing visit:

- BCVA loss <5 letters from reference visit, AND
- CRT <320 µm Heidelberg/<300 µm Cirrus or Topcon SD-OCT

Patients completing Week 36: 2q4 n=287; 8q8/3 n=278; 8q8/5 n=273. **Q4**, every 4 weeks; **Q8**, every 8 weeks.

Last Assigned Dosing Interval at Week 36



Mean number of active injections through Week 36[a]

2q4	8q8/3	8q8/5
8.5	6.0	6.7

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

Patients completing Week 36. [a]Full analysis set. **Q12**, every 12 weeks.

Ocular and Non-Ocular 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%)
Non-ocular 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%)

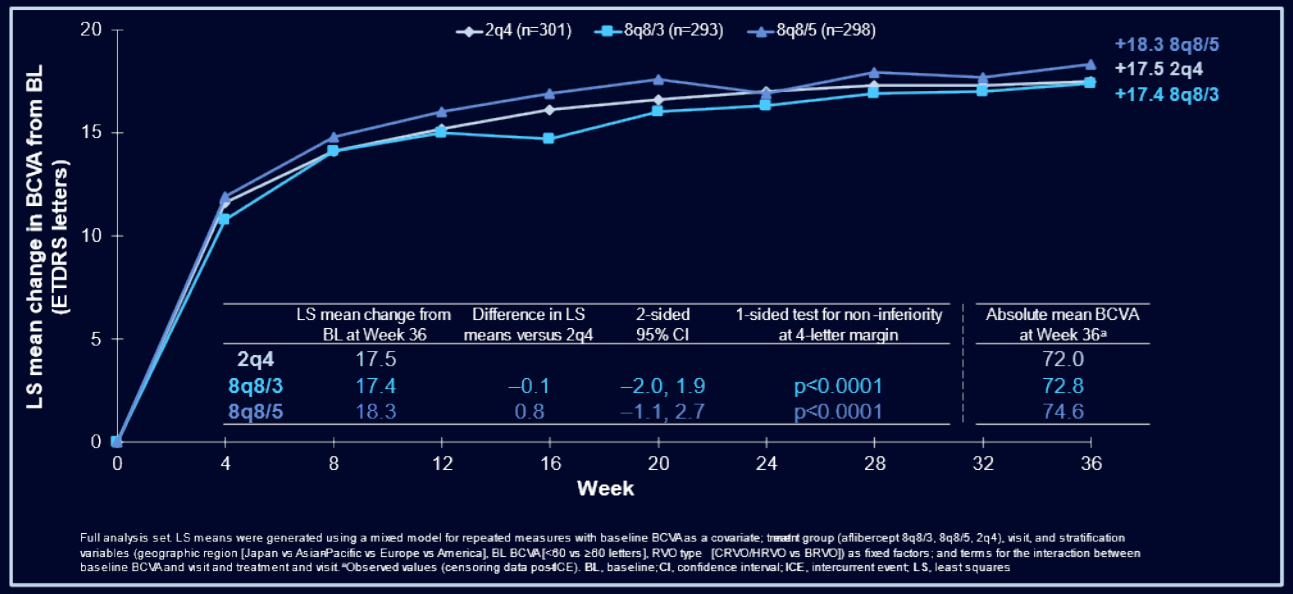
No cases of occlusive retinal vasculitis were reported

Aflibercept 8 mg was well-tolerated, consistent with the established safety of aflibercept 2 mg, with **no new safety signals**

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

QUASAR: Primary Endpoint Met

- Aflibercept 8 mg groups achieved **robust visual outcomes** and **non-inferior BCVA gains with fewer injections** compared with the aflibercept 2 mg group at Week 36
- Most patients in the aflibercept 8 mg groups **maintained their assigned Q8 intervals** through Week 36
- **Early, robust reductions in CRT** were maintained through Week 36
- Aflibercept 8 mg was well-tolerated, consistent with the established safety of aflibercept 2 mg, in patients with macular edema secondary to RVO, with **no new safety signals**



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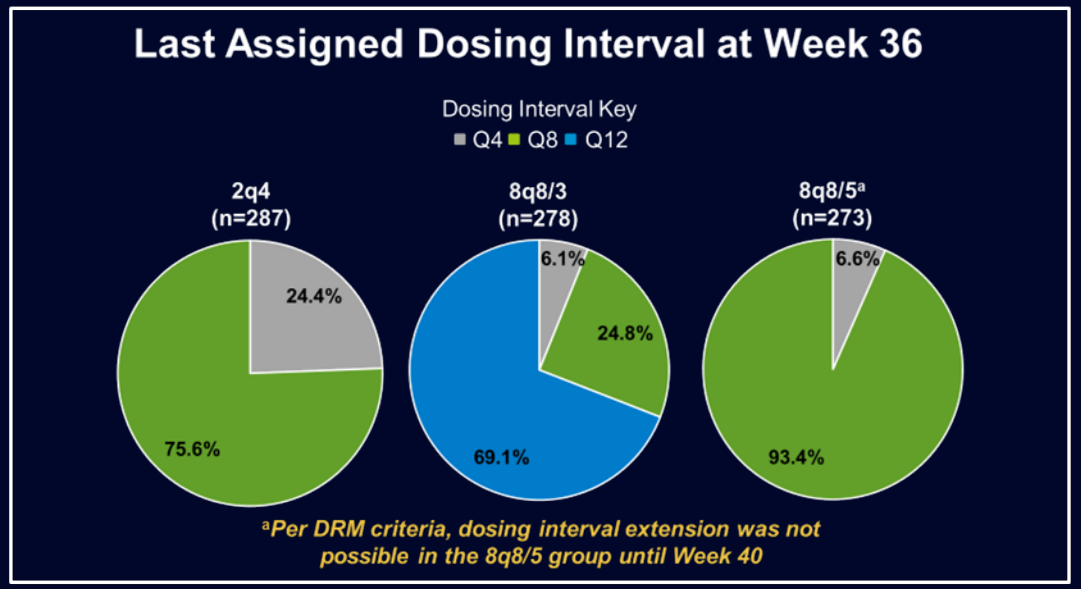

NOTE: p-values for the one-sided non-inferiority test at a margin of 4 letters (based on adjusted means derived using a mixed model for repeated measures).