Aflibercept 8 mg in Macular Edema Following Retinal Vein Occlusion: Week 64 Results From the QUASAR Trial

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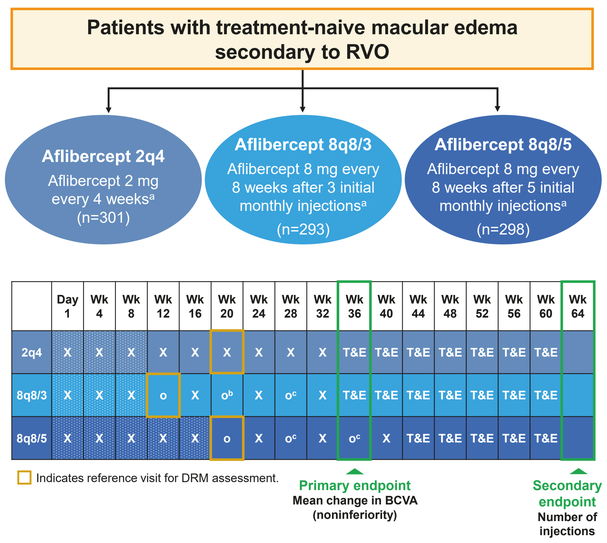
BACKGROUND & PURPOSE

- Anti-VEGF agents are the standard of care for macular edema following retinal vein occlusion (RVO).[1] However, they are administered at 4-week dosing intervals, which increases the treatment burden for patients and their caregivers
- The purpose of this study was to evaluate the efficacy and safety of intravitreal aflibercept 8 mg injections administered every 8 weeks, after 3 (8q8/3) or 5 (8q8/5) initial monthly injections, versus aflibercept 2 mg every 4 weeks (2q4) in patients with treatment-naive macular edema secondary to RVO

METHODS

- QUASAR (NCT05850520) was a 64-week multicenter, randomized, double-masked phase 3 trial of patients aged ≥18 years with macular edema secondary to RVO randomized 1:1:1 to 2q4, 8q8/3, or 8q8/5 (**Figure 1**)
- Patients who met prespecified dose-regimen modification (DRM) criteria could have their dosing intervals shortened or extended by 4-week increments. The minimum dosing interval was every 4 weeks for all patients (**Figure 1**)
- The primary efficacy endpoint was the least squares (LS) mean best-corrected visual acuity (BCVA) change from baseline in the aflibercept 8 mg versus 2 mg groups at Week 36, with a noninferiority margin of 4 letters
- The key secondary efficacy endpoint was number of active injections from baseline to Week 64
- Additional secondary endpoints included change from baseline in BCVA and central retinal thickness (CRT), proportion of patients with no intraretinal/subretinal fluid in the center subfield, treatment intervals, and safety through Week 64

Figure 1. Study Design



DRM for interval shortening

Dosing interval could be shortened by 4 weeks beginning at Week 16 for 8q8/3, Week 24 for 8q8/5, or Week 40 for 2q4 if both the following criteria were met at a dosing visit:

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

DRM for interval extension

Dosing interval could be 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 were met at a dosing visit:

- BCVA loss of <5 letters from reference visit[d], AND
- CRT <320 µm on Heidelberg Spectralis or <300 µm on Cirrus or Topcon SD OCT

Stippled boxes = initial treatment phase; X = active injection; o = sham injection. Note: Table does not reflect all dosing options once a patient's dosing interval was shortened.
[a]With opportunity for extension per DRM. [b]Active injection for patients meeting DRM criteria at Week 16. [c]Active injection for patients meeting DRM criteria from Week 16 for 8q8/3 or Week 24 for 8q8/5. [d]Reference is Week 12 for 8q8/3 and Week 20 for 8q8/5 and 2q4 (denoted by orange boxes on table).
SD OCT, spectral domain optical coherence tomography; T&E, treat and extend; Wk, week.

RESULTS

- Overall, 892 patients (2q4: n=301; 8q8/3: n=293; 8q8/5: n=298) were included. Mean age was 65.9 years, and the most common RVO type was branch retinal vein occlusion (BRVO) (52.4%), followed by central retinal vein occlusion (CRVO) (35.7%) and hemiretinal vein occlusion (HRVO) (12.0%) (**Table 1**)

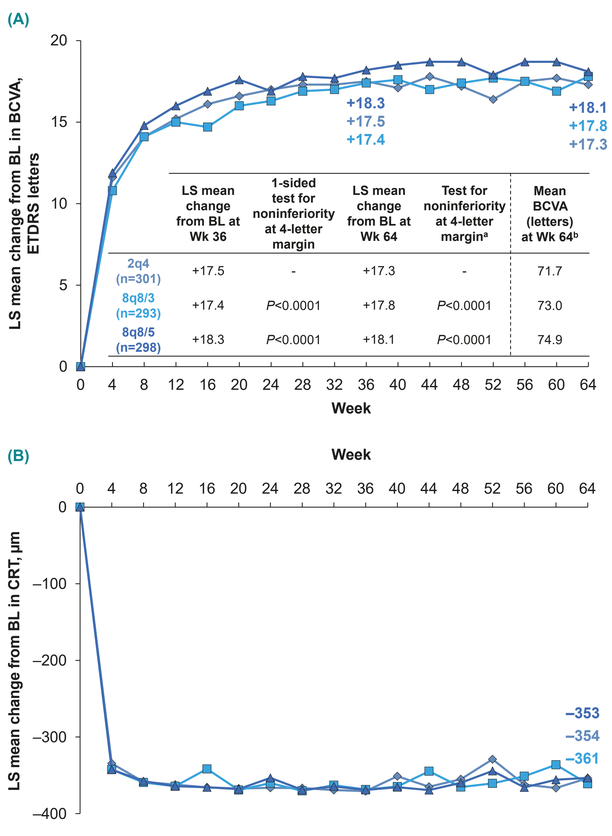
Table 1. Patient Disposition and Baseline Characteristics

	Aflibercept 2q4 (n=301)	Aflibercept 8q8/3 (n=293)	Aflibercept 8q8/5 (n=298)	Aflibercept Total (n=892)
Patients completing Week 36	287 (95.0)	278 (94.6)	273 (91.6)	838 (93.7)
Patients completing Week 64	270 (89.4)	269 (91.5)	256 (85.9)	795 (88.9)
Age, mean (SD), years	65.9 (11.7)	65.8 (11.5)	65.8 (11.5)	65.9 (11.6)
Female	144 (47.8)	136 (46.4)	146 (49.0)	426 (47.8)
RVO type[a]				
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, mean (SD), ETDRS letters	54.1 (14.3)	55.2 (13.6)	55.4 (13.4)	54.9 (13.8)
CRT, mean (SD), µm	651 (240)	626 (230)	609 (213)	629 (229)

Full analysis set. Data are n (%) unless otherwise indicated.
[a]Reading center assessed.
ETDRS, Early Treatment Diabetic Retinopathy Study; SD, standard deviation.

- Robust improvements in BCVA achieved with both 8q8/3 and 8q8/5 were comparable to that for 2q4 at Week 36 and were maintained through Week 64 (**Figure 2A**)
- Early, robust reductions in CRT observed with 8q8/3 and 8q8/5 were comparable to that for 2q4 and were maintained through Week 64 (**Figure 2B**)

Figure 2. LS Mean Change From Baseline Through Week 64 in BCVA (A) and CRT (B)

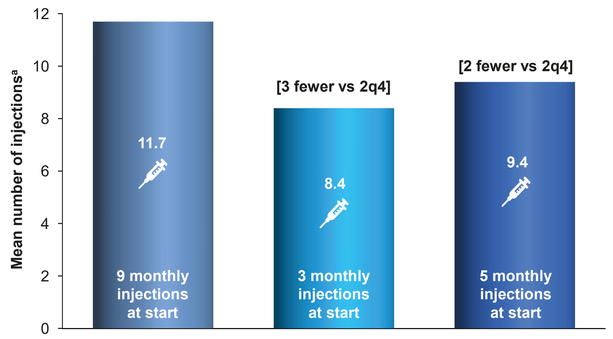


	LS mean change from BL at Wk 36	1-sided test for noninferiority at 4-letter margin	LS mean change from BL at Wk 64	Test for noninferiority at 4-letter margin[a]	Mean BCVA (letters) at Wk 64[b]
2q4 (n=301)	+17.5	-	+17.3	-	71.7
8q8/3 (n=293)	+17.4	*P*<0.0001	+17.8	*P*<0.0001	73.0
8q8/5 (n=298)	+18.3	*P*<0.0001	+18.1	*P*<0.0001	74.9

Full analysis set. LS means were generated using a mixed model for repeated measures with baseline BCVA (Panel A) or BL CRT (Panel B) as a covariate. The fixed factors were treatment arm (aflibercept 8q8/3, 8q8/5, or 2q4), visit, and stratification variables: geographic region (Japan, Asia-Pacific, Europe, or America), BL BCVA (<60 or ≥60 ETDRS letters), and RVO type (CRVO/HRVO or BRVO). The model also included terms for the interactions between BL BCVA (A) or BL CRT (B) and visit, and between treatment and visit.
[a]Nominal *P* value. [b]Observed values (censoring data following intercurrent event).
BL, baseline.

- Patients in both aflibercept 8q8/3 and 8q8/5 groups received significantly fewer injections than those in the aflibercept 2q4 group (**Figure 3**)

Figure 3. Active Injections With Aflibercept 8 mg Compared with Aflibercept 2 mg at Week 64

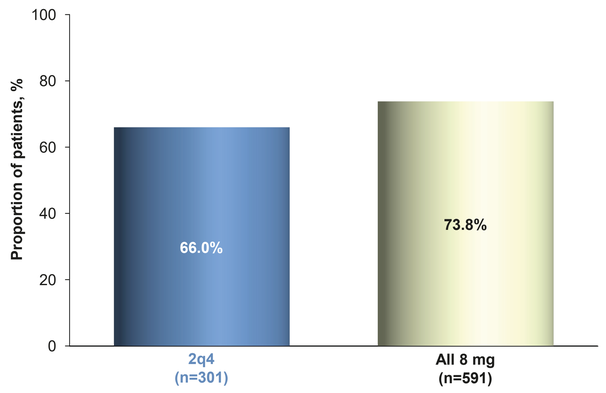


	LS mean difference vs 2q4 (95% CI)	*P* value
2q4 (n=301)	-	-
8q8/3 (n=293)	−3.2 (−3.5, −3.0)	<0.0001
8q8/5 (n=298)	−2.2 (−2.4, −2.0)	<0.0001

Full analysis set. Missing endpoint values imputed using a multiple imputation procedure. Based on a linear regression model (LS means and CI) and a non-parametric rank analysis of covariance (*P*-value), adjusted for BL BCVA, BL CRT, and stratification variables (geographic region [Japan, Asia-Pacific, Europe, or America], BCVA score [<60 vs ≥60 letters], and RVO type [CRVO/HRVO vs BRVO]), within the multiple imputation procedure.
[a]Full analysis set. Observed cases, patients completing Week 64.
CI, confidence interval.

- At Week 64, 66.0% of patients in the aflibercept 2 mg group and 73.8% of patients in the pooled 8 mg groups were fluid-free (**Figure 4**)

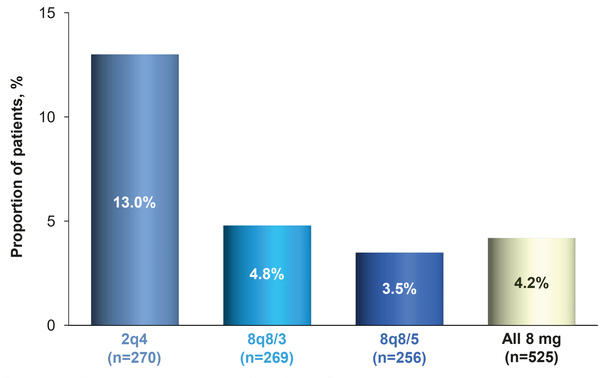
Figure 4. Proportion of Patients With No Retinal Fluid in the Center Subfield at Week 64



Full analysis set. Observed values (censoring data following intercurrent event). Fluid resolution defined as absence of both IRF and SRF in center subfield.
IRF, intraretinal fluid; SRF, subretinal fluid.

- Approximately 3 times fewer patients required every 4 weeks (Q4) dosing with aflibercept 8 mg versus 2 mg (**Figure 5**)

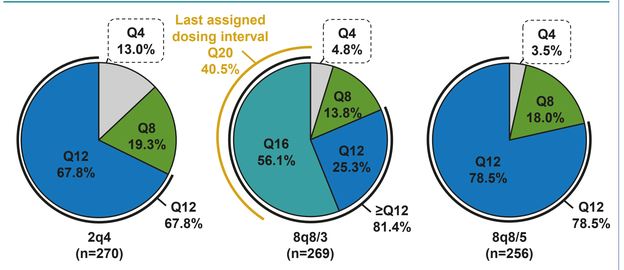
Figure 5. Proportion of Patients With Last Completed Dosing Interval of Q4 at Week 64



Patients in the full analysis set who completed Week 64 visit. Dosing intervals were extended by every 4 weeks from Week 32 for patients in the aflibercept 8q8/3 and 2q4 groups and from Week 40 for those in the aflibercept 8q8/5 group if prespecified DRM criteria were met.

- Approximately 80% of patients treated with aflibercept 8 mg had a last completed dosing interval of Q12 or longer, and 40.5% of patients in the 8q8/3 group had a last assigned dosing interval of Q20 (**Figure 6**)

Figure 6. Patient Distribution by Last Completed Dosing Interval at Week 64



Patients in the full analysis set who completed Week 64 visit. Per study design, extension was possible starting from Week 32 with 2q4 and 8q8/3 and from Week 40 with 8q8/5.
Q12, every 12 weeks; Q16, every 16 weeks; Q20, every 20 weeks.

- The safety profile of aflibercept 8 mg was consistent with the established safety profile for aflibercept 2 mg and 8 mg (**Table 2**)

Table 2. Ocular and Non-ocular Safety Through Week 64

	Aflibercept 2q4 (n=301)	Aflibercept 8q8/3 (n=293)	Aflibercept 8q8/5 (n=298)	All Aflibercept 8 mg (n=591)
Ocular TEAEs in the study eye, %	42.2	45.7	39.6	42.6
Serious ocular TEAEs in the study eye, %	2.7	1.7	1.7	1.7
Intraocular inflammation in the study eye, %	1.7	1.4	0.7	1.0
Anterior chamber cell	0.3	0	0	0
Eye inflammation	0.3	0	0	0
Iritis	0	0.3	0	0.2
Uveitis	0	0	0.7	0.3
Vitritis	0	0.7	0	0.3
Endophthalmitis	1.0	0.3	0	0.2
Serious non-ocular TEAEs, %	12.0	11.3	11.1	11.2
APTC events, %	2.0	0.7	2.3	1.5
Deaths, %	1.0	0.7	1.7	1.2

Safety analysis set. APTC, Antiplatelet Trialists' Collaboration; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- **Improvements in BCVA and CRT** achieved at Week 36 were **maintained through Week 64** across all treatment groups, with **up to 3.2 fewer injections** with aflibercept 8 mg compared with aflibercept 2 mg
- At Week 64, **more patients treated with aflibercept 8 mg versus 2 mg were fluid-free** in the center subfield
- At Week 64, ~3-fold **fewer patients treated with aflibercept 8 mg versus 2 mg had a last completed interval of Q4**, despite interval extension being permitted for the aflibercept 2 mg group
- At Week 64, **approximately 80%** of patients in the aflibercept 8 mg groups **achieved ≥Q12 dosing**, with 40.5% of patients in the aflibercept 8q8/3 group having a last assigned interval of Q20
- **The safety of aflibercept 8 mg in** patients with RVO through Week 64 of the QUASAR trial was **comparable to the known safety profile** for aflibercept 2 mg and 8 mg

REFERENCES

1. Kovach JL et al. *Ophthalmology.* 2025;132(4):303-343.

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Poster presented by Jordana G. Fein, MD, email: jgorenmd@gmail.com, at the RWC 2026 Meeting, May 14-17, 2026