Aflibercept 8 mg in Treatment-naïve Macular Edema Secondary to Retinal Vein Occlusion: Primary Endpoint Results from the QUASAR Study

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Disclosures

- **Seenu M. Hariprasad** reports being a consultant or a member of the Speakers Bureau for AbbVie, Alimera Sciences/ANI, Astellas, Bayer, Biogen, Harrow, Iveric Bio, Regeneron Pharmaceuticals, Inc., and Sun Pharma
    - **VC** receives grants from Bayer, Novartis, and Roche; and serves on advisory boards for Alcon, Apellis, Bayer, Boehringer Ingelheim, Novartis, and Roche. **YC** serves as a speaker for AbbVie, Bayer, Chengdu Kanghong, Novartis, and Roche. **AC** receives consultant fees from Alcon, Apellis, Astellis, Bayer, Novartis, Opthea, Roche, and Zeiss; and grant funding from Bayer, Novartis, and Roche. **MK** receives financial support from Alcon Japan, Hoya Surgical Optics, Otsuka Pharmaceutical, Santen, and Senju; compensation or travel expenses from Alcon Japan, Bayer, Chugai, Hoya Surgical Optics, Kowa, Santen, Senju, and Wakamoto Pharma; and consultant fees from Chugai, Daisel, Hoya Surgical Optics, Senju, and SONY. **SL** is an employee, investor, and patent holder of Bayer Consumer Care AG. **LB** and **ZH** are employees of Bayer Consumer Care AG. **SS** and **FM** are employees of Bayer AG. **AJB** and **AA** are employees of Regeneron Pharmaceuticals, Inc. **RK** receives research funding from Alimera, Bayer, Chengdu Kanghong, Novartis, Opthea, and Roche; and serves as a speaker for AbbVie, Alimera, Apellis, Bayer, Heidelberg Engineering, Novartis, and Roche
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- This study includes research conducted on human patients. Institutional Review Board/Institutional Ethics Committee approval was obtained prior to study initiation
- Medical writing support, under the direction of the author, was provided by ApotheCom and funded by Bayer Consumer Care AG, Basel, Switzerland, in accordance with Good Publication Practice (GPP) guidelines (*Ann Intern Med.* 2022;175:1298–1304)
- Aflibercept 8 mg is currently not on label for treating macular edema due to retinal vein occlusion, however applications seeking approval of aflibercept 8 mg for macular edema due to retinal vein occlusion, including central, branch, and hemiretinal vein occlusion, have been submitted to the FDA and EMA
- Contents of this presentation have been updated from the original presentation at the Angiogenesis Meeting 2025, Virtual Edition, February 8, 2025

QUASAR: Study Design

An ongoing, multi-center, randomized, double-masked, Phase 3 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
Mean change in BCVA (non-inferiority)

	Day 1	W4	W8	W12	W16	W20	W24	W28	W32	W36
2q4	X	X	X	X	X	X	X	X	X	T&E
8q8/3	X	X	X	o	X	o[b]	X	o[c]	X	T&E
8q8/5	X	X	X	X	X	o	X	o[c]	X	o[d]

DRM for interval shortening

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

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

DRM for interval extension

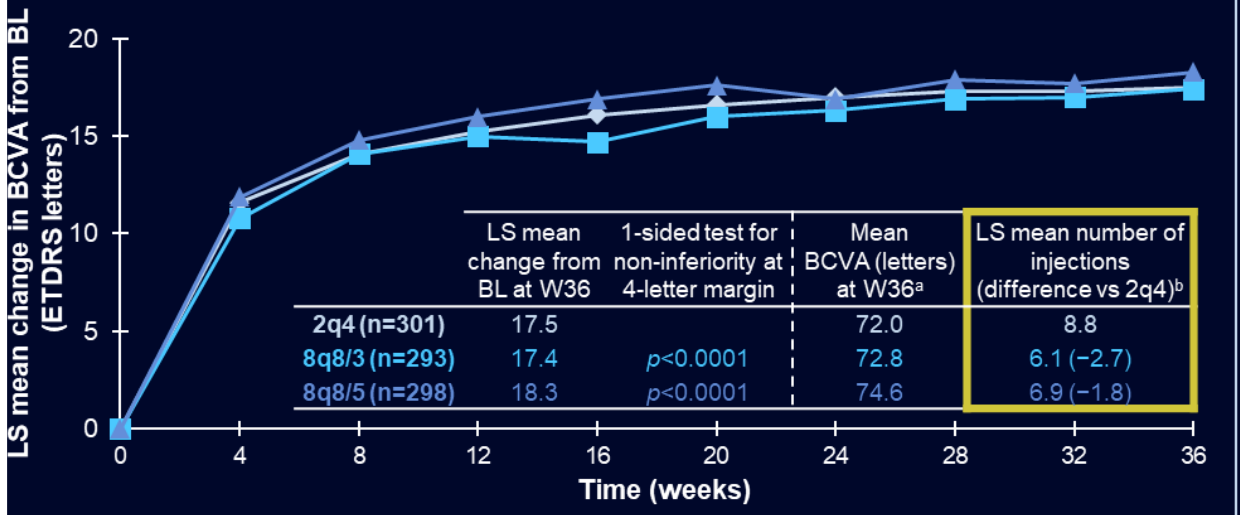
Dosing interval extended by 4 weeks starting at Week 32 for 8q8/3 and 2q4 and at Week 40 for 8q8/5 if both the following criteria are met at a dosing visit:

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

The primary efficacy endpoint was change from baseline in BCVA at Week 36, with a non-inferiority margin of 4 letters. 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 is shortened. [a]With opportunity for extension per DRM. [b]Active injection for participants meeting DRM criteria at Week 16. [c]Active injection for participants meeting DRM criteria at Week 16 or 24. [d]Active injection for participants meeting DRM at Weeks 16, 24, or 32. [e]Reference is Week 12 for 8q8/3 and Week 20 for 8q8/5 and 2q4 (denoted by green boxes on table). **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; **BCVA**, best-corrected visual acuity; **CRT**, central subfield retinal thickness; **DRM**, dose-regimen modification; **RVO**, retinal vein occlusion; **SD-OCT**, spectral domain-optical coherence tomography; **T&E**, treat and extend; **W**, week.

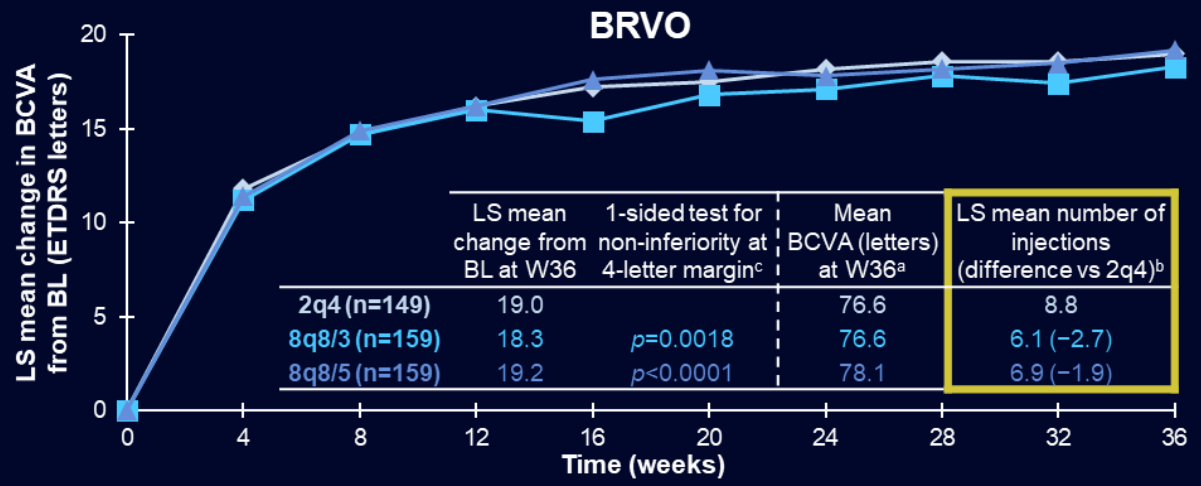
Both Aflibercept 8 mg Groups Achieved Non-inferior BCVA Gains Compared to Aflibercept 2 mg at Week 36, with Fewer Injections Overall and Across RVO Subtypes

Overall RVO Population



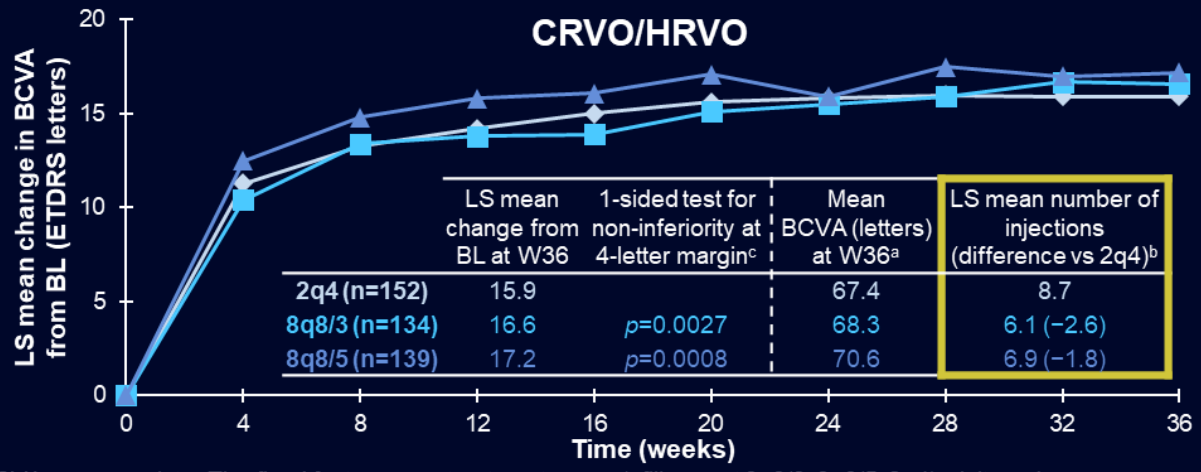
	LS mean change from BL at W36	1-sided test for non-inferiority at 4-letter margin	Mean BCVA (letters) at W36[a]	LS mean number of injections (difference vs 2q4)[b]
2q4 (n=301)	17.5		72.0	8.8
8q8/3 (n=293)	17.4	*p*<0.0001	72.8	6.1 (−2.7)
8q8/5 (n=298)	18.3	*p*<0.0001	74.6	6.9 (−1.8)

BRVO



	LS mean change from BL at W36	1-sided test for non-inferiority at 4-letter margin[c]	Mean BCVA (letters) at W36[a]	LS mean number of injections (difference vs 2q4)[b]
2q4 (n=149)	19.0		76.6	8.8
8q8/3 (n=159)	18.3	*p*=0.0018	76.6	6.1 (−2.7)
8q8/5 (n=159)	19.2	*p*<0.0001	78.1	6.9 (−1.9)

CRVO/HRVO

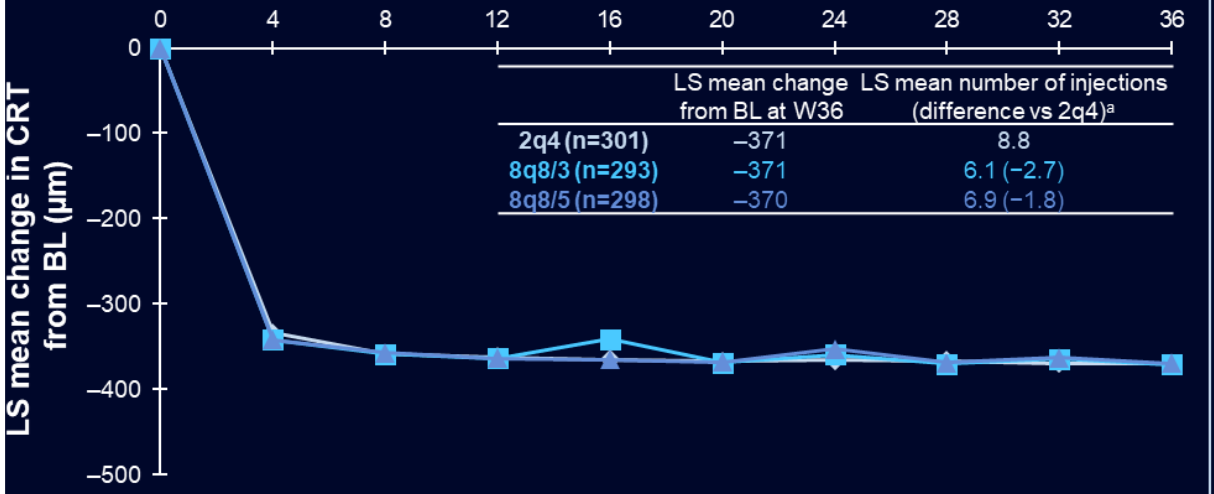


	LS mean change from BL at W36	1-sided test for non-inferiority at 4-letter margin[c]	Mean BCVA (letters) at W36[a]	LS mean number of injections (difference vs 2q4)[b]
2q4 (n=152)	15.9		67.4	8.7
8q8/3 (n=134)	16.6	*p*=0.0027	68.3	6.1 (−2.6)
8q8/5 (n=139)	17.2	*p*=0.0008	70.6	6.9 (−1.8)

Full analysis set. LS means were generated using a mixed model for repeated measures with baseline BCVA as a covariate. The fixed factors were treatment group (aflibercept 8q8/3, 8q8/5, 2q4); visit; and stratification variables: geographic region (Japan, Asian-Pacific, Europe, America), BL BCVA (<60 vs ≥60 letters), and, for the overall RVO population analysis only, RVO type (CRVO/HRVO vs BRVO). The model also included terms for the interactions between baseline BCVA and visit, and between treatment and visit. [a]Observed values (censoring data post intercurrent event). [b]Missing endpoint values imputed using a multiple imputation procedure. Based on a linear regression model. Non-parametric rank analysis of covariance, adjusted for BL BCVA, BL CRT, and stratification variables (geographic region [Japan vs APAC vs Europe vs America], BCVA score [>60 vs ≥60], RVO type [CRVO/HRVO vs BRVO], within the multiple imputation procedure. [c]Nominal p-values. **BL**, baseline; **BRVO**, branch retinal vein occlusion; **CRVO**, central retinal vein occlusion; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **HRVO**, hemiretinal vein occlusion; **LS**, least squares.

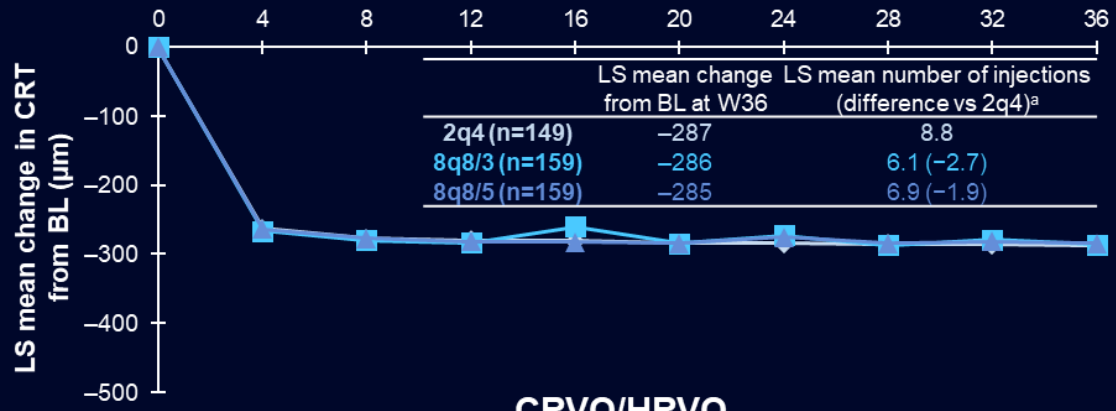
Both Aflibercept 8 mg Groups Achieved Robust CRT Reductions Compared to Aflibercept 2 mg at Week 36, with Fewer Injections Overall and Across RVO Subtypes

Overall RVO Population



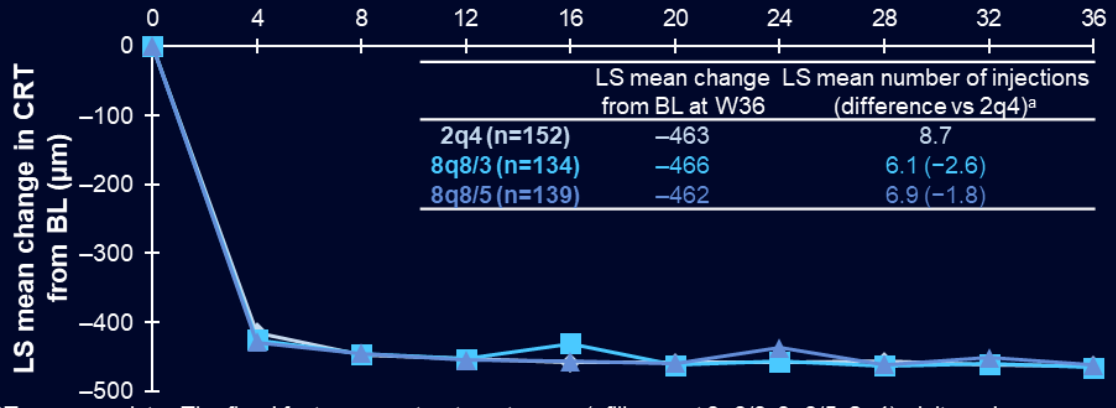
	LS mean change from BL at W36	LS mean number of injections (difference vs 2q4)[a]
2q4 (n=301)	−371	8.8
8q8/3 (n=293)	−371	6.1 (−2.7)
8q8/5 (n=298)	−370	6.9 (−1.8)

BRVO



	LS mean change from BL at W36	LS mean number of injections (difference vs 2q4)[a]
2q4 (n=149)	−287	8.8
8q8/3 (n=159)	−286	6.1 (−2.7)
8q8/5 (n=159)	−285	6.9 (−1.9)

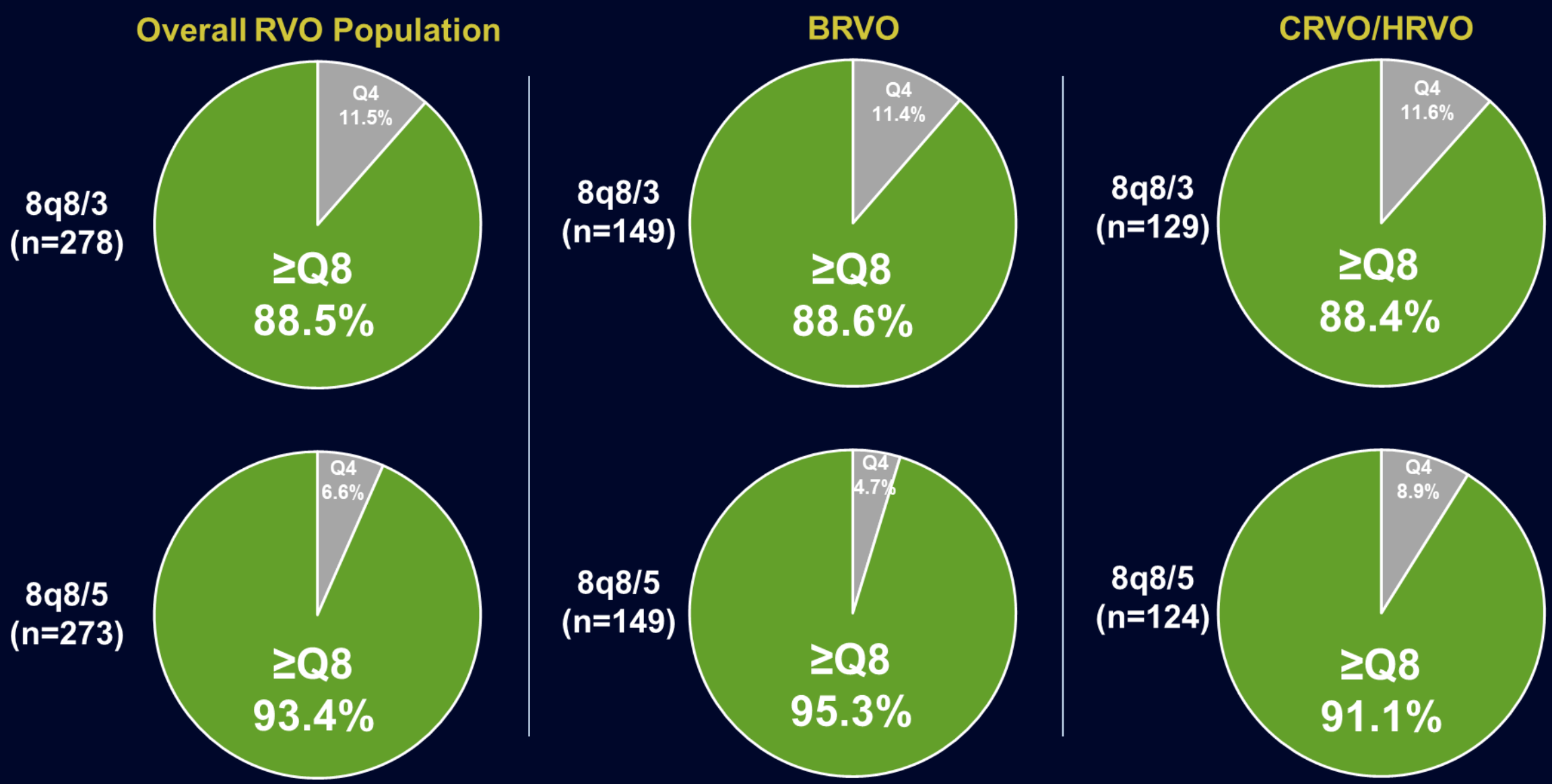
CRVO/HRVO



	LS mean change from BL at W36	LS mean number of injections (difference vs 2q4)[a]
2q4 (n=152)	−463	8.7
8q8/3 (n=134)	−466	6.1 (−2.6)
8q8/5 (n=139)	−462	6.9 (−1.8)

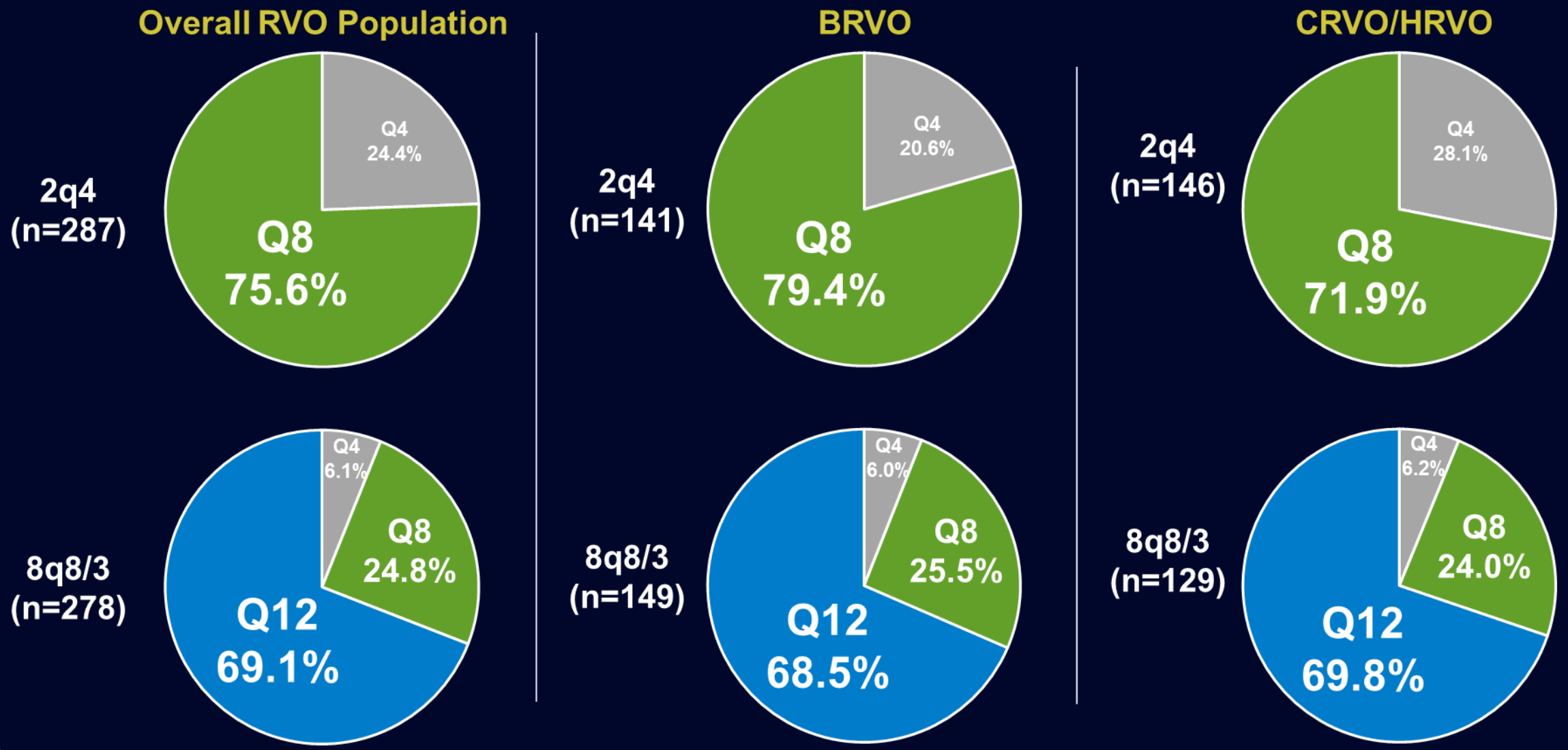
Full analysis set. LS means were generated using a mixed model for repeated measures with baseline CRT as a covariate. The fixed factors were treatment group (aflibercept 8q8/3, 8q8/5, 2q4), visit; and stratification variables: geographic region (Japan, Asian-Pacific, Europe, America), BL BCVA (<60 vs ≥60 letters), and, for the overall RVO population analysis only, RVO type (CRVO/HRVO vs BRVO). The model also included terms for the interaction between baseline CRT and visit, and treatment and visit. [a]Missing endpoint values imputed using a multiple imputation procedure. Based on a linear regression model. Non-parametric rank analysis of covariance, adjusted for BL BCVA, BL CRT, and stratification variables (geographic region [Japan vs APAC vs Europe vs America], BCVA score [>60 vs ≥60], RVO type [CRVO/HRVO vs BRVO], within the multiple imputation procedure.

Participants with ≥Q8 Dosing Intervals for the Overall Population, BRVO and CRVO/HRVO Subtypes at Week 36



Safety analysis set. Patients completing Week 36.

Last Assigned Dosing Interval at Week 36 for Patients Eligible for Interval Extension: Overall Population, BRVO and CRVO/HRVO Subtypes



Safety analysis set. Patients completing Week 36. Per study design, dosing interval extension was not possible in the 8q8/5 group until Week 40.

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 in the study eye, n (%)	85 (28.2)	103 (35.2)	86 (28.9)	189 (32.0)
Ocular SAEs in the study eye, n (%)	8 (2.7)	3 (1.0)	4 (1.3)	7 (1.2)
Intraocular inflammation in the study eye, 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

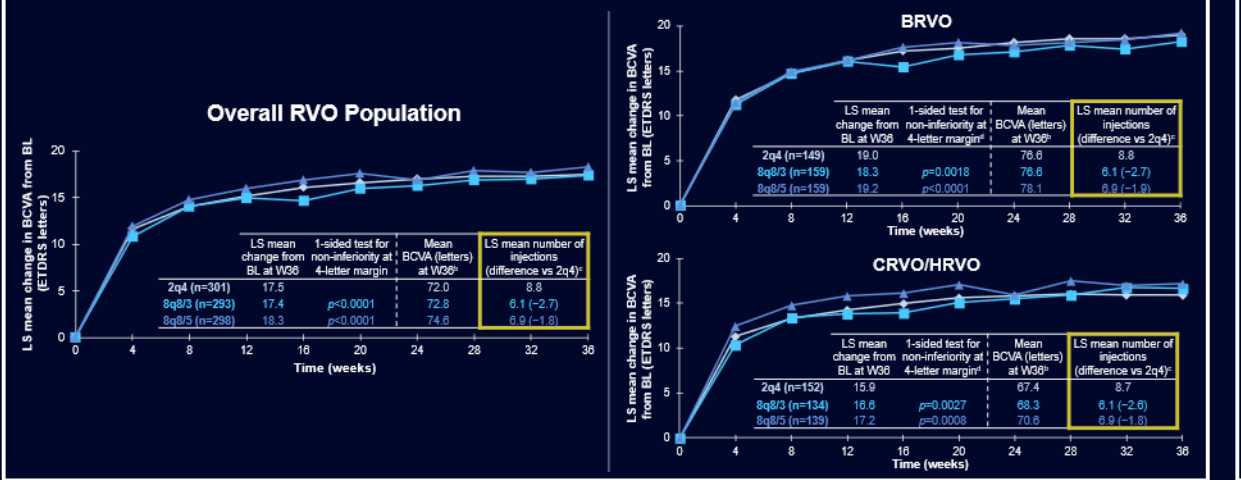
Aflibercept 8 mg was well tolerated, consistent with the established safety of aflibercept 2 mg and 8 mg

Safety analysis set. **APTC**, Anti-Platelet Trialists' Collaboration; **SAE**, serious adverse event; **TEAE**, treatment-emergent adverse event.

QUASAR: Paradigm Shift in the Treatment of RVO

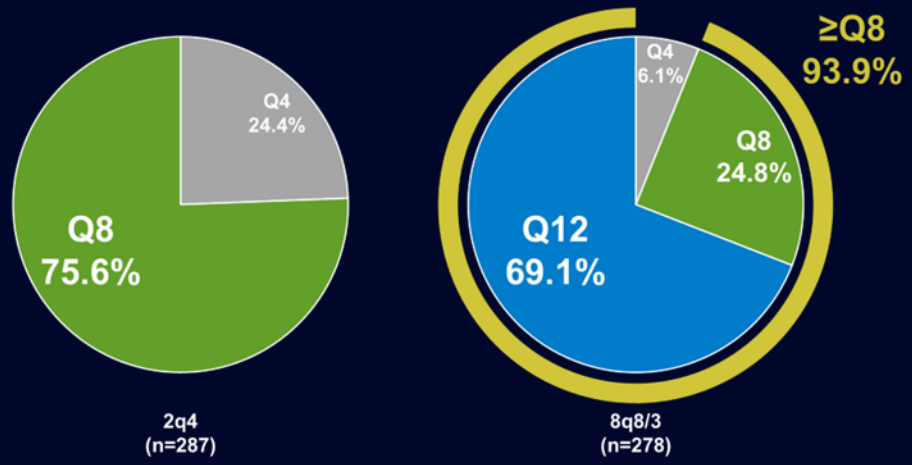
- Aflibercept 8q8/3 and 8q8/5 groups achieved **non-inferior BCVA gains and robust reductions in CRT** with fewer injections than with the aflibercept 2q4 at Week 36, overall and across BRVO and CRVO/HRVO subtypes
- Approximately **94% of patients in the aflibercept 8q8/3 group achieved a last assigned dosing interval of ≥8 weeks,** overall and across BRVO and CRVO/HRVO subtypes
- The safety profile of aflibercept 8 mg in patients with macular edema secondary to RVO was **consistent with the established safety profile of aflibercept 2 mg and 8 mg**

Both Aflibercept 8 mg Groups Achieved Non-inferior BCVA Gains Compared to Aflibercept 2 mg at Week 36, with Fewer Injections Overall and Across RVO Subtypes[a]



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

Overall RVO Population



[a]Full analysis set. LS means were generated using a mixed model for repeated measures with baseline BCVA as a covariate. The fixed factors were treatment group (aflibercept 8q8/3, 8q8/5, 2q4); visit; and stratification variables: geographic region (Japan, Asian-Pacific, Europe, America), BL BCVA (<60 vs ≥60 letters), and, for the overall RVO population analysis only, RVO type (CRVO/HRVO vs BRVO). The model also included terms for the interactions between baseline BCVA and visit, and between treatment and visit. [b]Observed values (censoring data post ICE). [c]Missing endpoint values imputed using a multiple imputation procedure. Based on a linear regression model. Non-parametric rank analysis of covariance, adjusted for BL BCVA, BL CRT, and stratification variables (geographic region [Japan vs APAC vs Europe vs America], BCVA score [>60 vs ≥60], RVO type [CRVO/HRVO vs BRVO], within the multiple imputation procedure. [d]Nominal p-values. [e]Safety analysis set. Patients completing Week 36.