



Aflibercept 8 mg in Treatment-naïve Macular Edema Secondary to Retinal Vein Occlusion: Primary Endpoint Results from the Phase 3 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
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- This study included 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 the EMA

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

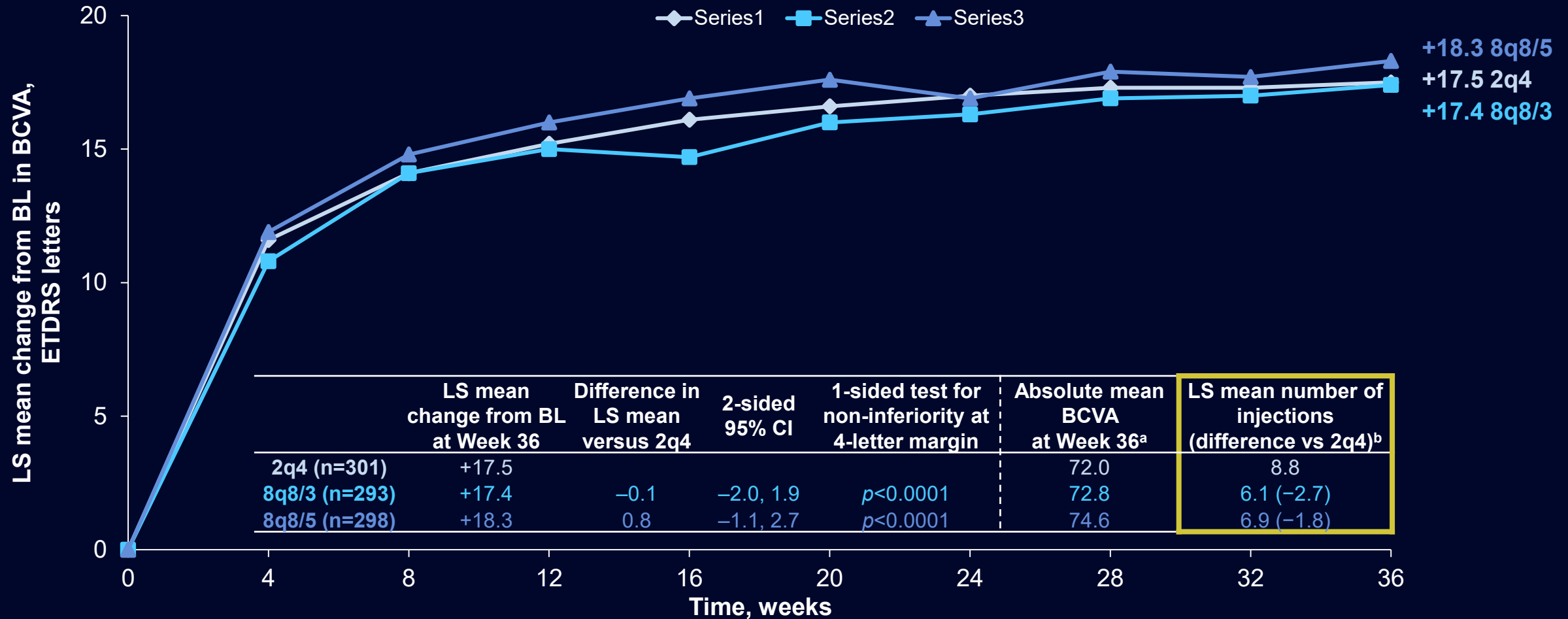
DRM for interval extension

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

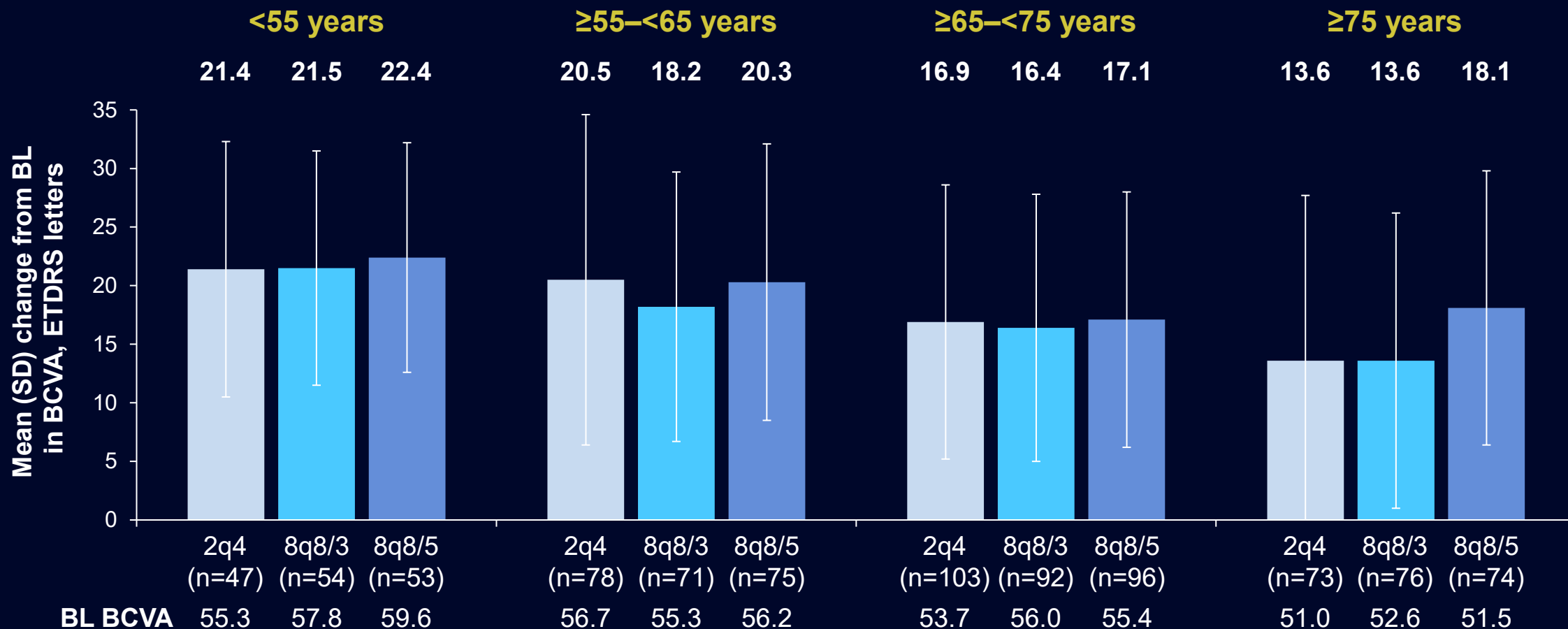
The primary efficacy endpoint was change from baseline in BCVA at Week 36, with a non-inferiority margin of 4 letters. Stippled boxes = initial treatment phase; X = active injection; o = sham injection. Note: Table does not reflect all dosing options once a patient's dosing interval is shortened. ^aWith opportunity for extension per DRM. ^bActive injection for participants meeting DRM criteria at Week 16. ^cActive injection for participants meeting DRM criteria at Week 16 or 24. ^dActive injection for participants meeting DRM at Weeks 16, 24, or 32. ^eReference 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.

Aflibercept 8 mg Groups Achieved Non-inferior BCVA Gains Compared to Aflibercept 2 mg at Week 36, with Fewer Injections

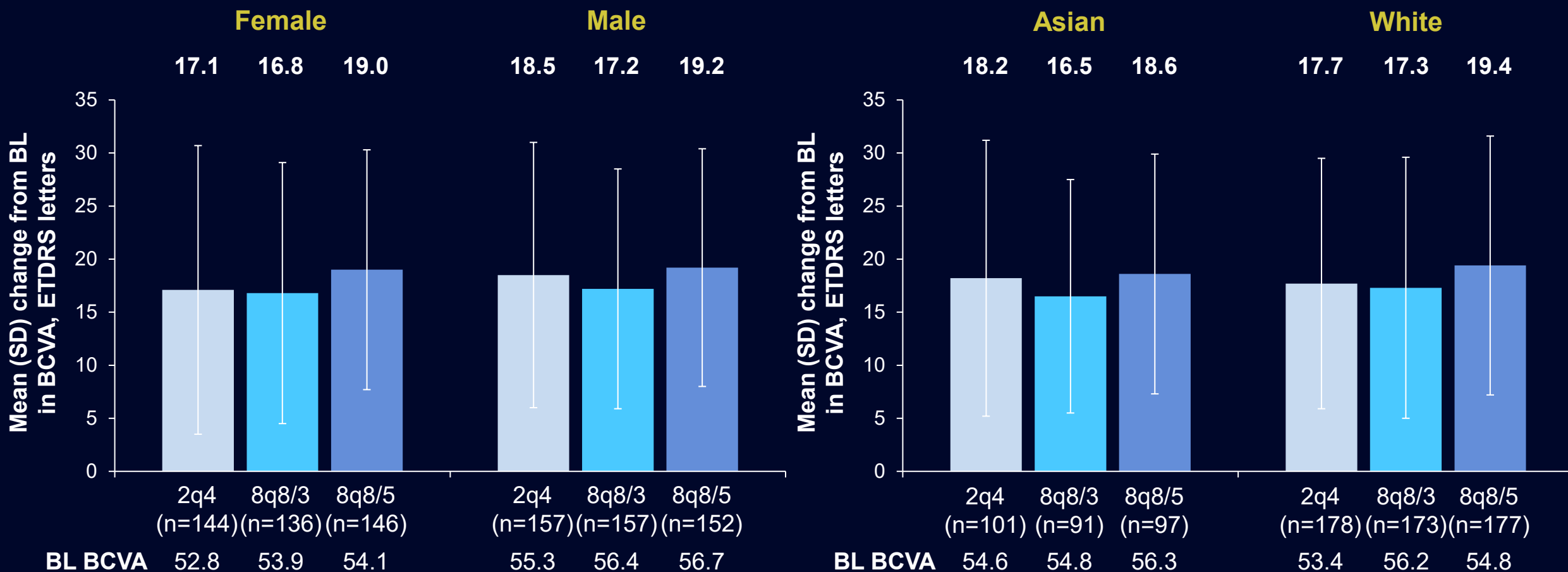


Full analysis set. LS means were generated using a mixed model for repeated measures with baseline BCVA as a covariate. The fixed factors were treatment group (aflibercept 8q8/3, 8q8/5, 2q4); visit; and stratification variables: geographic region (Japan, Asia-Pacific, Europe, America), BL BCVA (<60 vs ≥60 letters), and RVO type (CRVO/HRVO vs BRVO). The model also included terms for the interactions between baseline BCVA and visit, and between treatment and visit. ^aObserved values (censoring data post intercurrent event). ^bMissing endpoint values imputed using a multiple imputation procedure. Estimates based on a linear regression model, within the multiple imputation procedure, adjusted for BL BCVA, BL CRT, and stratification variables (geographic region [Japan vs Asia-Pacific vs Europe vs America], BCVA score [>60 vs ≥60], RVO type [CRVO/HRVO vs BRVO]). **BL**, baseline; **BRVO**, branch retinal vein occlusion; **CI**, confidence interval; **CRVO**, central retinal vein occlusion; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **HRVO**, hemiretinal vein occlusion; **LS**, least squares.

Mean Change in BCVA at Week 36 by Age

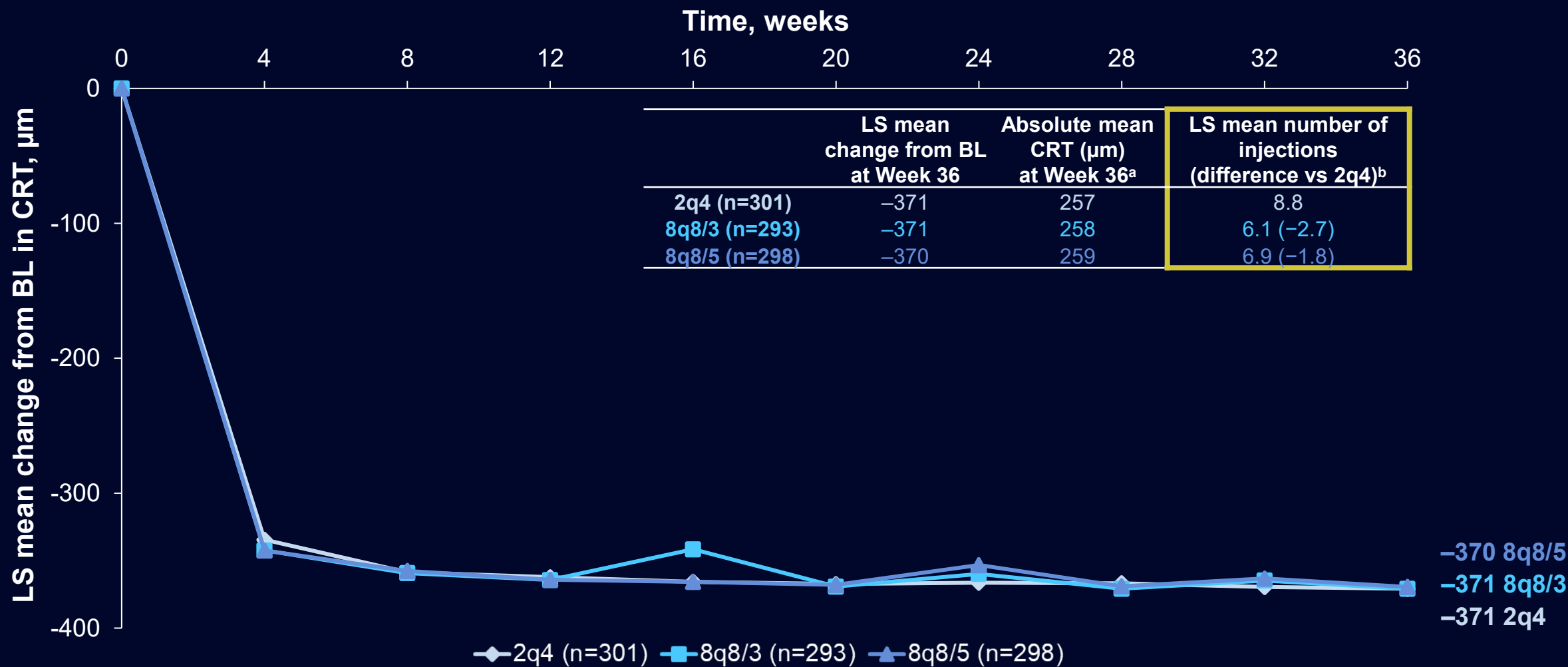


Mean Change in BCVA at Week 36 by Sex and Race^a



Full analysis set. Observed values (censoring data post intercurrent event). ^aThe subgroup Black or African American race could not be evaluated due to small sample size (8, 7, and 9 patients in the 2q4, 8q8/3 and 8q8/5 groups, respectively).

Both Aflibercept 8 mg Groups Achieved Robust CRT Reductions Compared to Aflibercept 2 mg at Week 36, with Fewer Injections

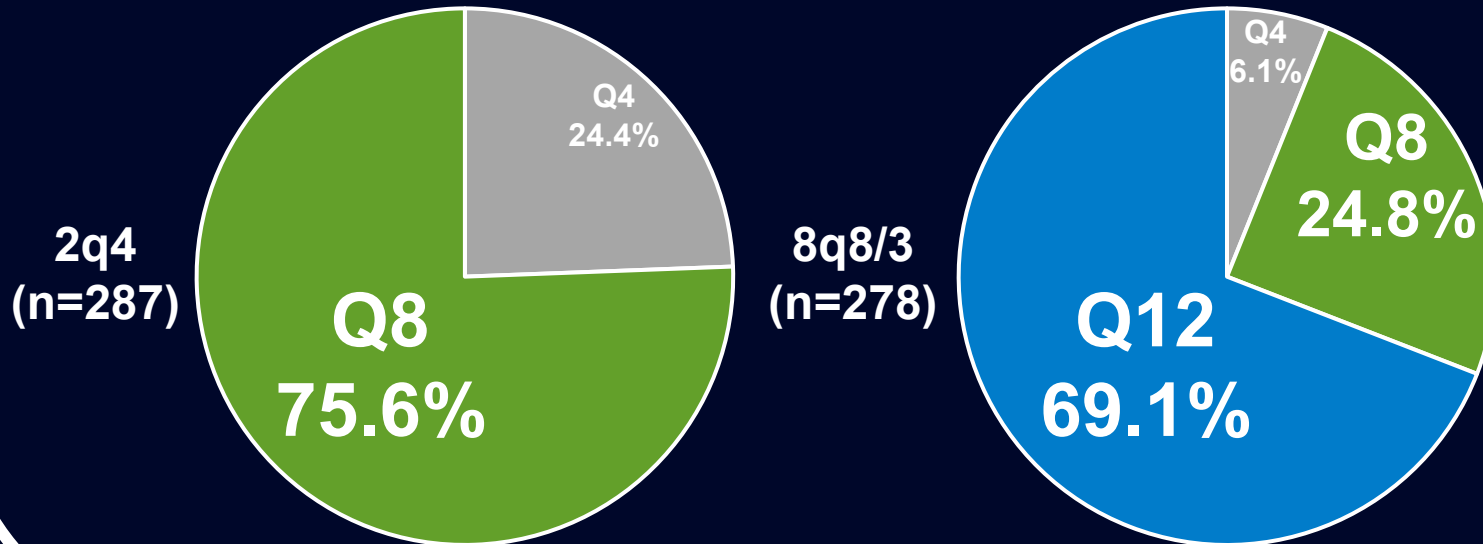
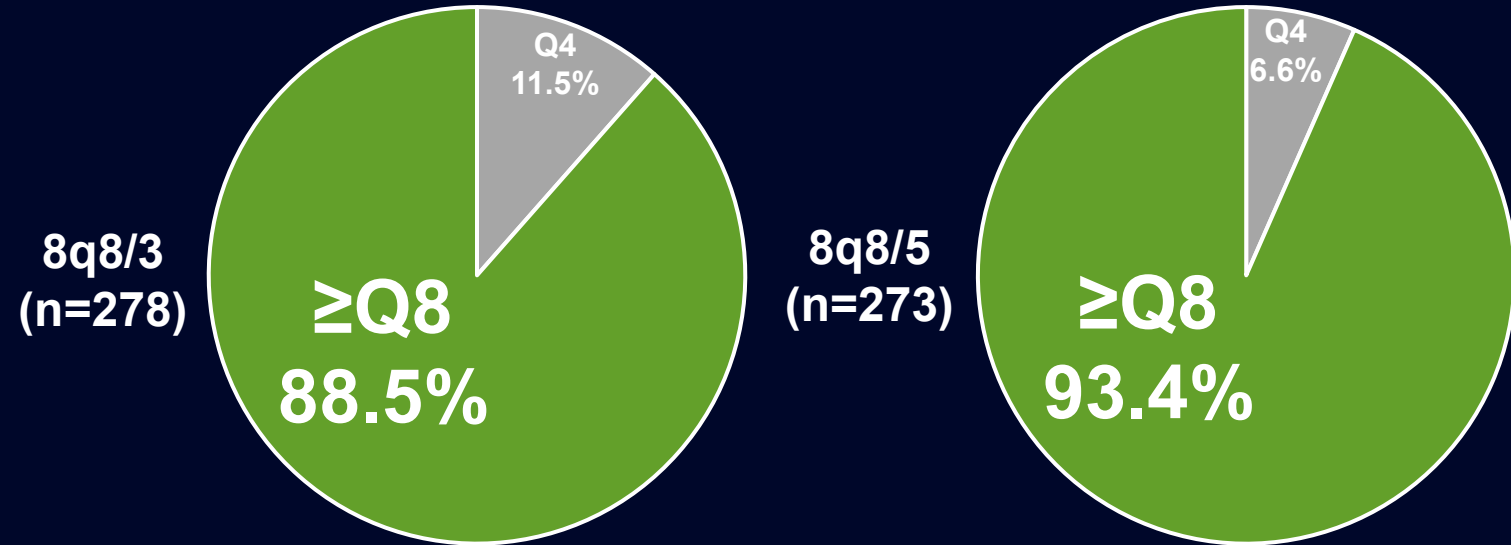


Full analysis set. LS means were generated using a mixed model for repeated measures with baseline CRT as a covariate; treatment group (aflibercept 8q8/3, 8q8/5, 2q4), visit, and stratification variables (geographic region [Japan vs Asia-Pacific vs Europe vs America], BL BCVA [<60 vs ≥ 60 letters], RVO type [CRVO/HRVO vs BRVO]) as fixed factors; and terms for the interaction between baseline CRT and visit and treatment and visit. ^aObserved values (censoring data post intercurrent event). ^bMissing endpoint values imputed using a multiple imputation procedure. Estimates based on a linear regression model, within the multiple imputation procedure, adjusted for BL BCVA, BL CRT, and stratification variables (geographic region [Japan vs Asia-Pacific vs Europe vs America], BCVA score [>60 vs ≥ 60], RVO type [CRVO/HRVO vs BRVO]).

Aflibercept Dosing Intervals Through Week 36

Maintained Dosing Interval^a

Most patients in the 8q8 groups maintained a Q8 dosing interval through Week 36



Last Assigned Dosing Interval^b

Most patients in the 8q8/3 and 2q4 groups who were eligible for interval extension had a last assigned dosing interval of ≥Q8 at Week 36

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

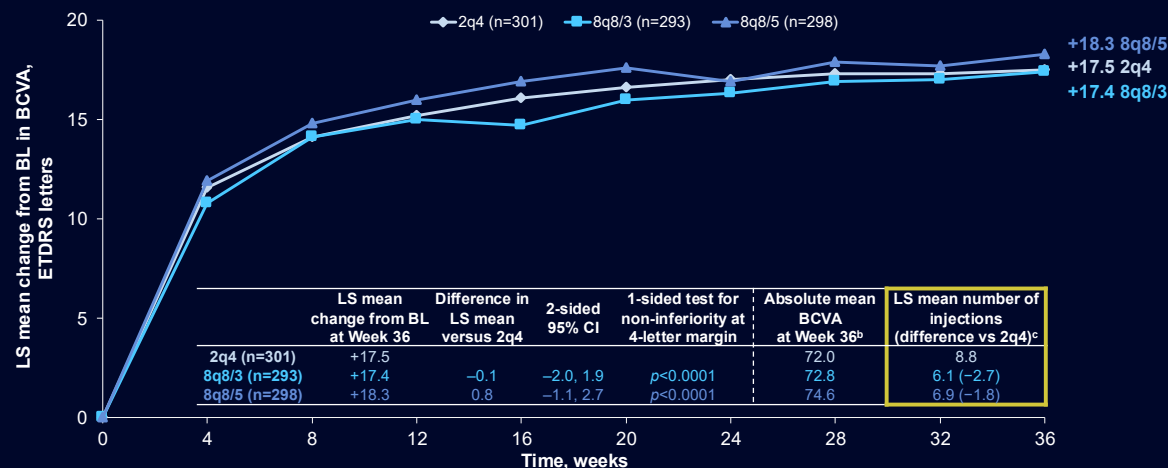
Aflibercept 8 mg had a safety profile consistent with the established safety profile of aflibercept 2 mg and 8 mg

QUASAR: Paradigm Shift in the Treatment of RVO with Aflibercept 8 mg

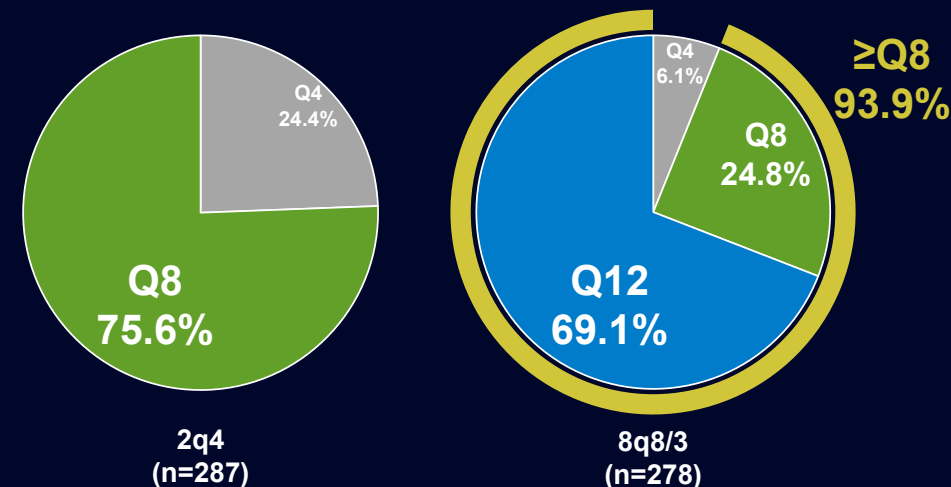


- Aflibercept 8q8/3 and 8q8/5 groups achieved **non-inferior BCVA gains and robust reductions in CRT**, with fewer injections than in the aflibercept 2q4 group at Week 36
- Aflibercept 8 mg **achieved clinically meaningful BCVA gains from baseline** at Week 36 in patients with macular edema secondary to RVO **across evaluable subgroups of age, sex, and race** with fewer injections than in the aflibercept 2q4 group
- Approximately **94% of patients in the aflibercept 8q8/3 group achieved a last assigned dosing interval of ≥ 8 weeks**
- 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**

Aflibercept 8 mg Groups Achieved Non-inferior BCVA Gains Compared to Aflibercept 2 mg at Week 36,^a with Fewer Injections



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



^aFull 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, Asia-Pacific, Europe, America), BL BCVA (<60 vs ≥ 60 letters), and RVO type (CRVO/HRVO vs BRVO). The model also included terms for the interactions between baseline BCVA and visit, and between treatment and visit. ^bObserved values (censoring data post intercurrent event). ^cMissing endpoint values imputed using a multiple imputation procedure. Estimates based on a linear regression model, within the multiple imputation procedure, adjusted for BL BCVA, BL CRT, and stratification variables (geographic region [Japan vs Asia-Pacific vs Europe vs America], BCVA score [>60 vs ≥ 60], RVO type [CRVO/HRVO vs BRVO]). ^dSafety analysis set. Patients completing Week 36.

References



- Pielen, A, et al. *Clin Ophthalmol*. 2017;11:1533–1540.
- Korobelnik, J-F, et al. *Am J Ophthalmol*. 2021;227:106–115.