Aflibercept 8 mg for Retinal Vein Occlusion: Outcomes of the QUASAR Phase 3 Randomized Trial by RVO Type, CRVO/HRVO, or BRVO

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Disclosures

- **Charles Wykoff** is a consultant and receives research support from Bayer, EyeBiotech, Genentech, Kodiak, Novartis, and Regeneron Pharmaceuticals, Inc.
    - **LB** is a former employee of Bayer Consumer Care AG. **RG** and **ZH** are employees of Bayer Consumer Care AG. **SS**, **FM**, **TM**, and **TN** are employees of Bayer AG. **AJB**, **AA**, **FS**, and **TS** are employees of Regeneron Pharmaceuticals, Inc. **SL** is an employee, investor, and patent holder of Bayer Consumer Care AG
- The QUASAR trial (NCT05850520) was 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 included research conducted on human patients. Institutional Review Board/Institutional Ethics Committee approval was obtained prior to study initiation
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- 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
- The QUASAR group wishes to thank all patients and investigators of the QUASAR trial

QUASAR: Study Design

A 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 the reference visit, AND
- >50 µm increase in CRT from the 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 the 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.

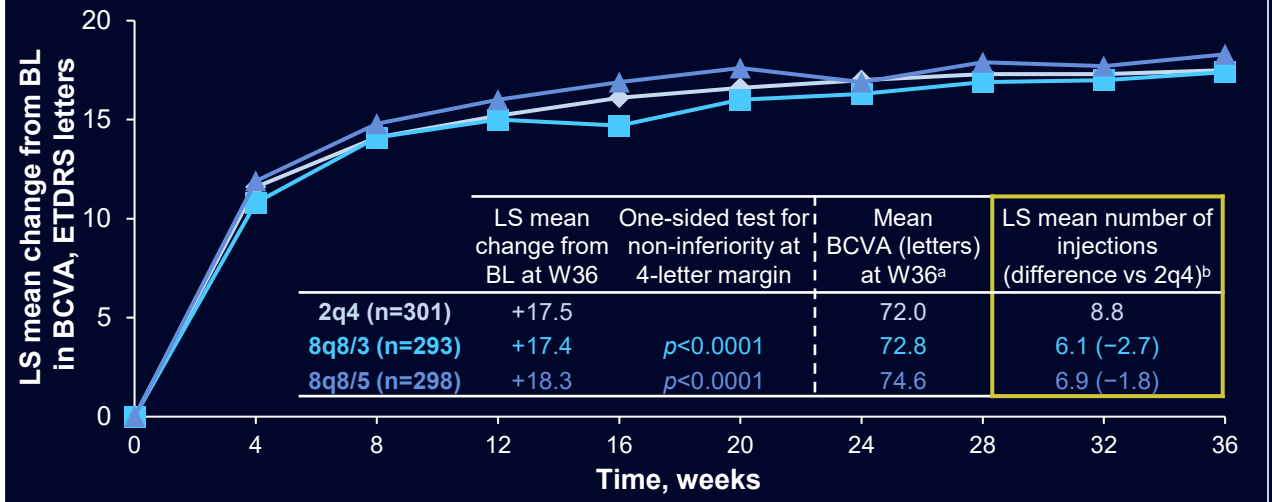
Baseline Demographics and Disease Characteristics

	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 subtype, 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)
BRVO subtype	57.3 (13.2)	58.6 (11.5)	58.5 (11.5)	58.2 (12.0)
CRVO/HRVO subtype	51.0 (14.7)	51.3 (14.8)	51.8 (14.5)	51 (14.7)
CRT, µm[c]	651 (240)	626 (230)	609 (213)	629 (229)
BRVO subtype	553 (170)	549 (170)	541 (161)	547 (167)
CRVO/HRVO subtype[d]	748 (260)	718 (257)	688 (238)	719 (253)

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. [d]2q4, n=151; Total=424. **BRVO**, branch retinal vein occlusion; **CRVO**, central retinal vein occlusion; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **HRVO**, hemiretinal vein occlusion; **SD,** standard deviation.

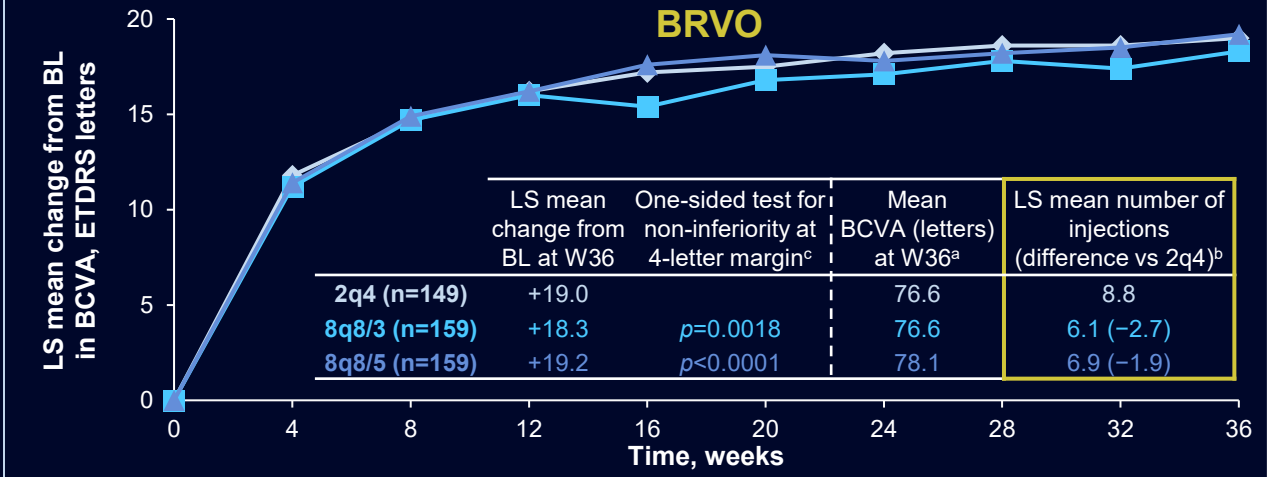
Both Aflibercept 8 mg Groups Achieved Non-inferior BCVA Gains Compared to Aflibercept 2 mg at Week 36, with Fewer Injections Overall and Consistent Results Across RVO Subtypes

Overall RVO population



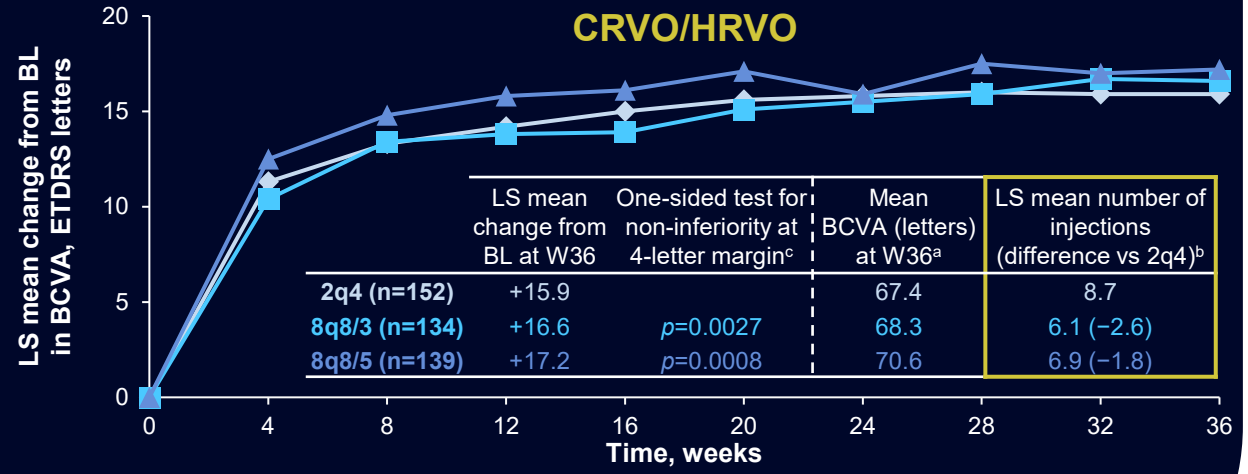
	LS mean change from BL at W36	One-sided test for non-inferiority at 4-letter margin	Mean BCVA (letters) at W36[a]	LS mean number of injections (difference vs 2q4)[b]
2q4 (n=301)	+17.5		72.0	8.8
8q8/3 (n=293)	+17.4	*p*<0.0001	72.8	6.1 (−2.7)
8q8/5 (n=298)	+18.3	*p*<0.0001	74.6	6.9 (−1.8)

BRVO



	LS mean change from BL at W36	One-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

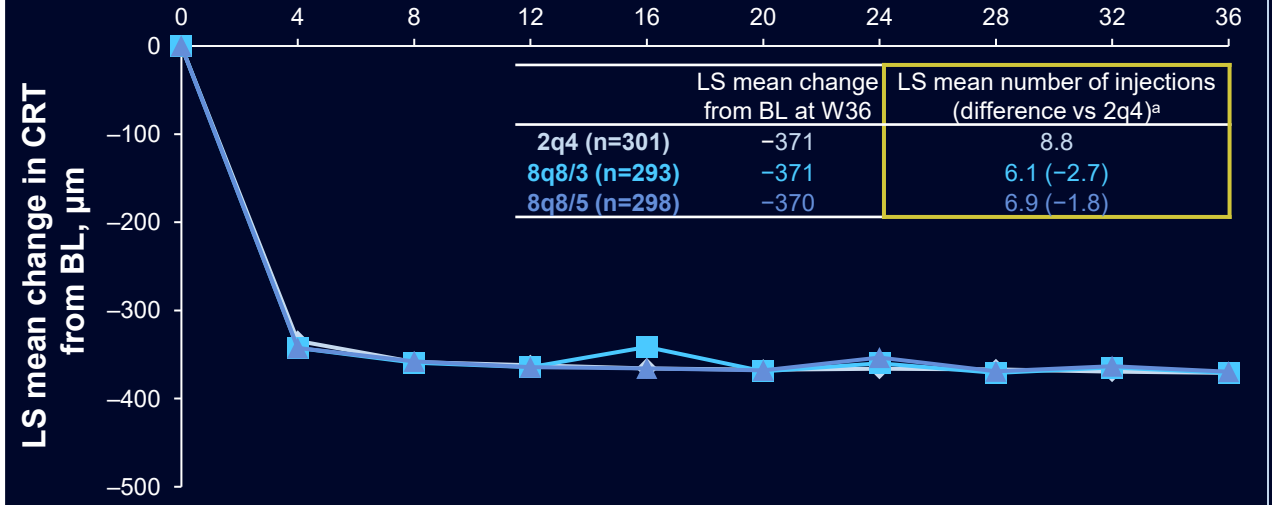


	LS mean change from BL at W36	One-sided test for non-inferiority at 4-letter margin[c]	Mean BCVA (letters) at W36[a]	LS mean number of injections (difference vs 2q4)[b]
2q4 (n=152)	+15.9		67.4	8.7
8q8/3 (n=134)	+16.6	*p*=0.0027	68.3	6.1 (−2.6)
8q8/5 (n=139)	+17.2	*p*=0.0008	70.6	6.9 (−1.8)

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, Asia-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. 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]). [c]Nominal *p*-values. **BL**, baseline; **CI**, confidence interval; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **LS**, least squares.

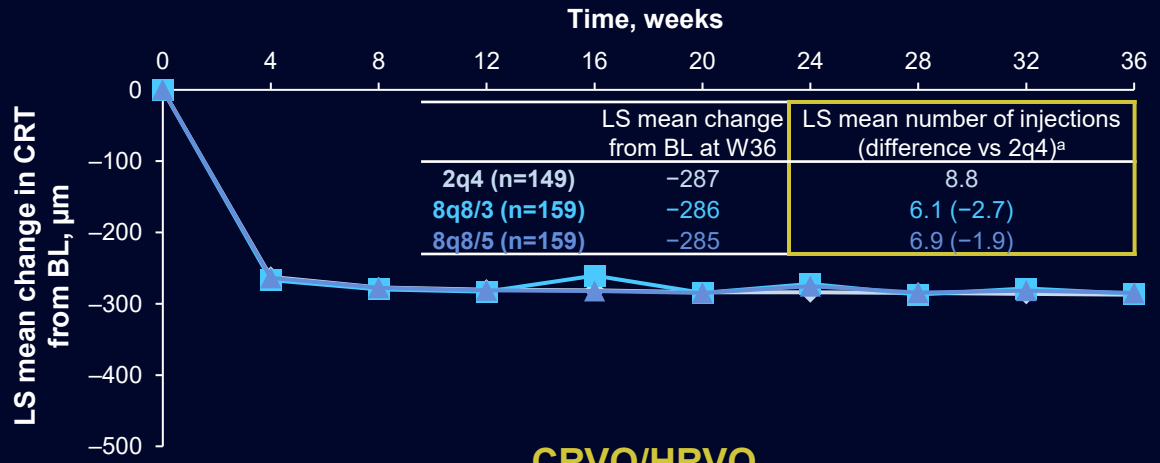
Both Aflibercept 8 mg Groups Achieved Robust CRT Reductions Compared to Aflibercept 2 mg at Week 36, with Fewer Injections

Overall RVO population



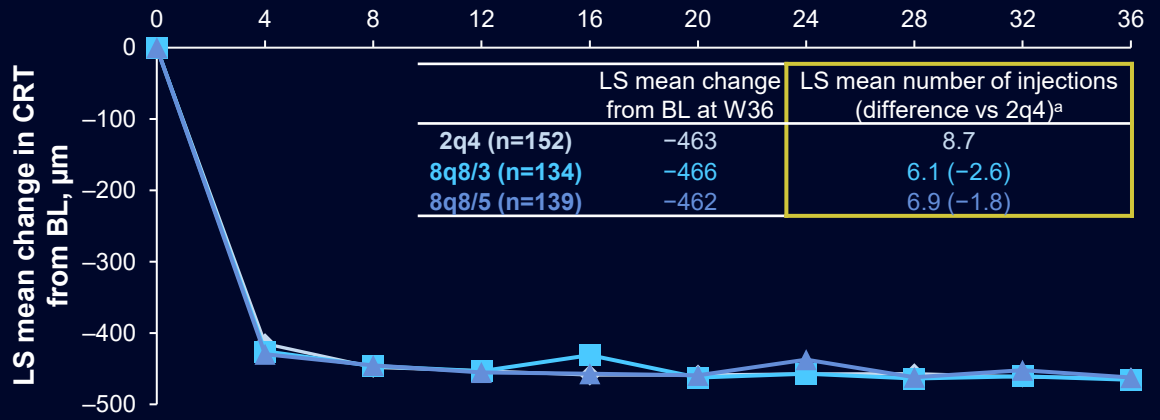
	LS mean change from BL at W36	LS mean number of injections (difference vs 2q4)[a]
2q4 (n=301)	−371	8.8
8q8/3 (n=293)	−371	6.1 (−2.7)
8q8/5 (n=298)	−370	6.9 (−1.8)

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 Asian-Pacific vs Europe vs America], BCVA score [>60 vs ≥60], RVO type [CRVO/HRVO vs BRVO], within the multiple imputation procedure.

Comparable BCVA Gains Achieved Across Treatment Groups, with Fewer Injections Across Baseline CRT Tertiles by RVO Subtypes

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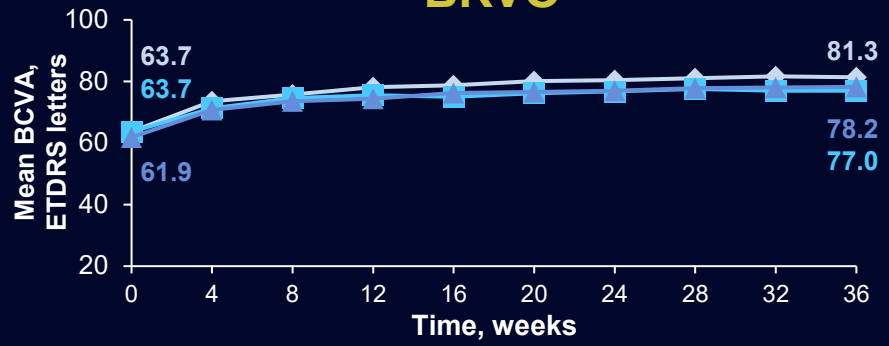
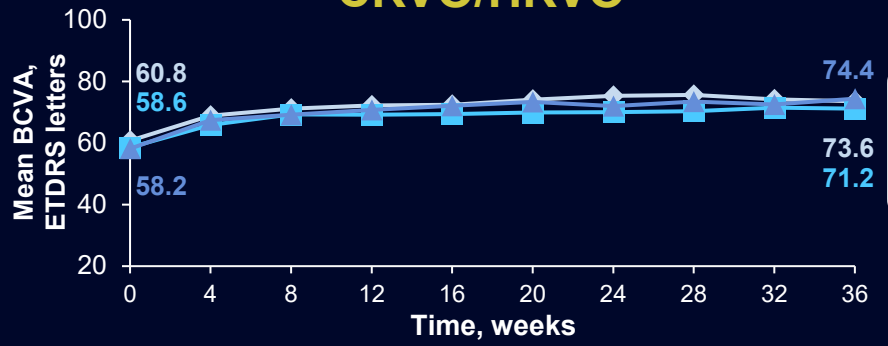
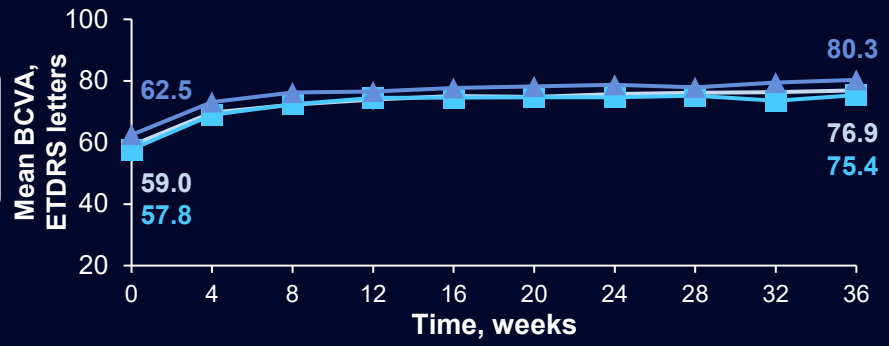
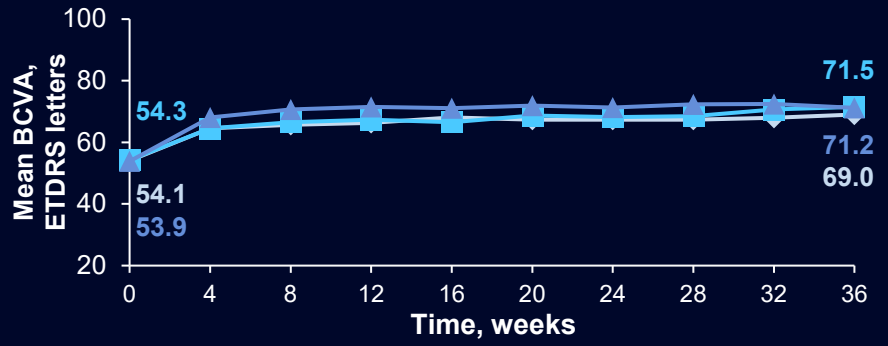
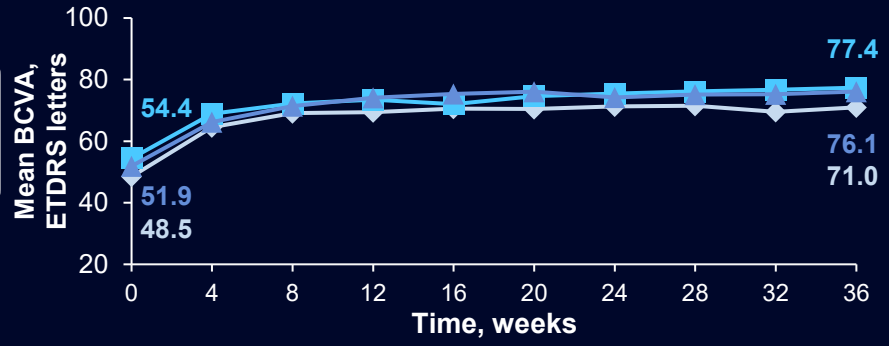
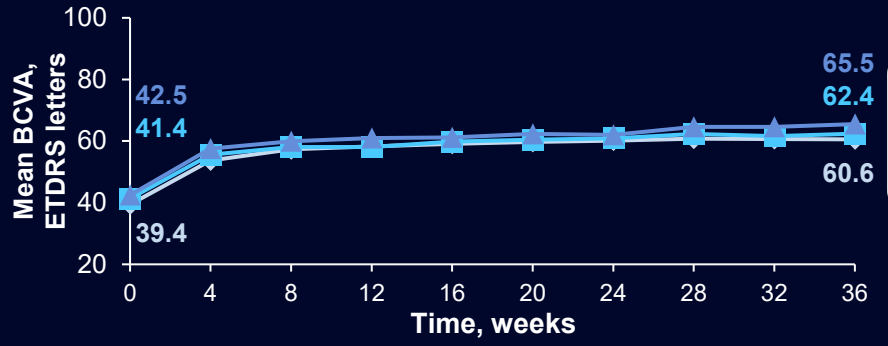
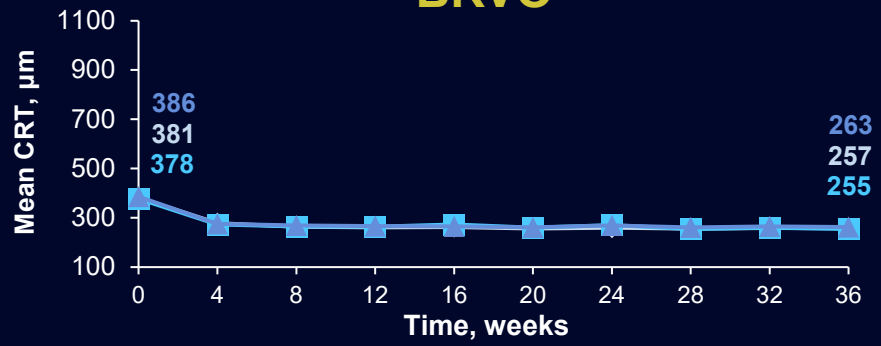
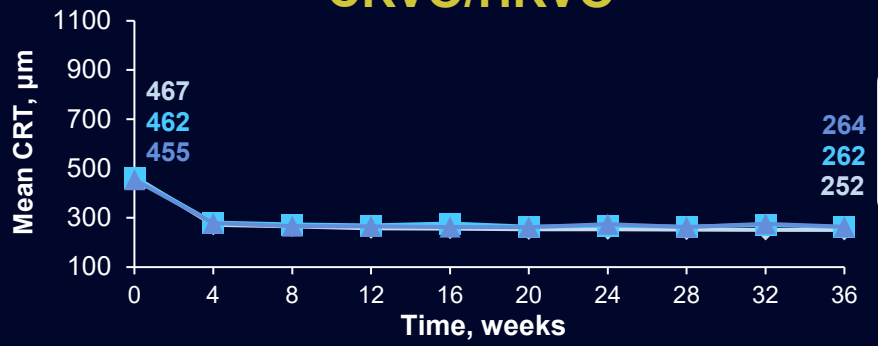
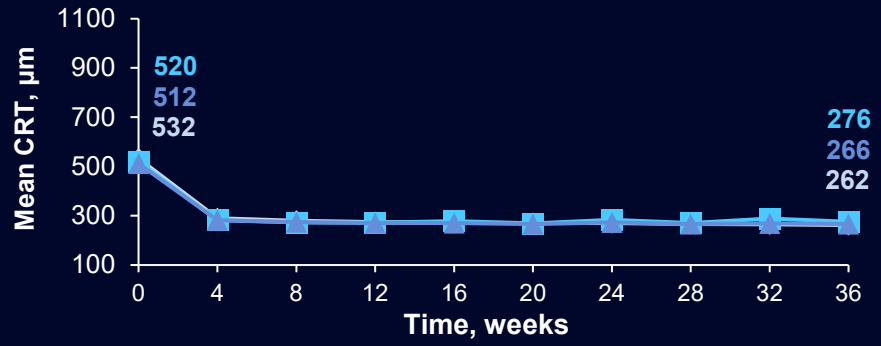
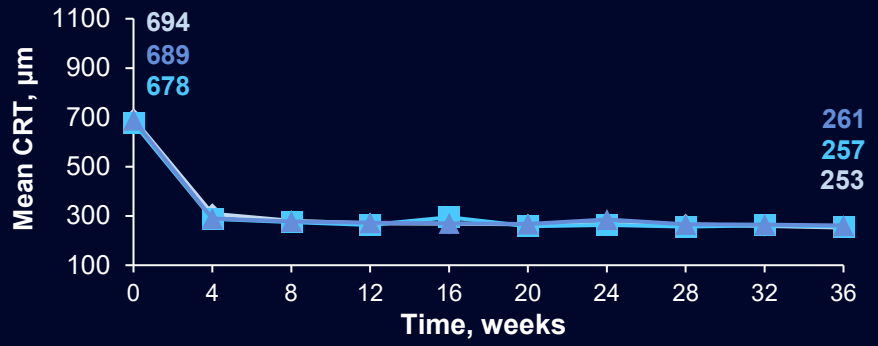
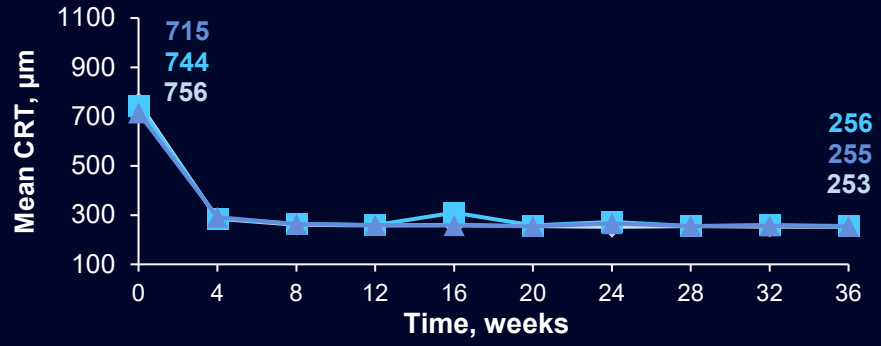
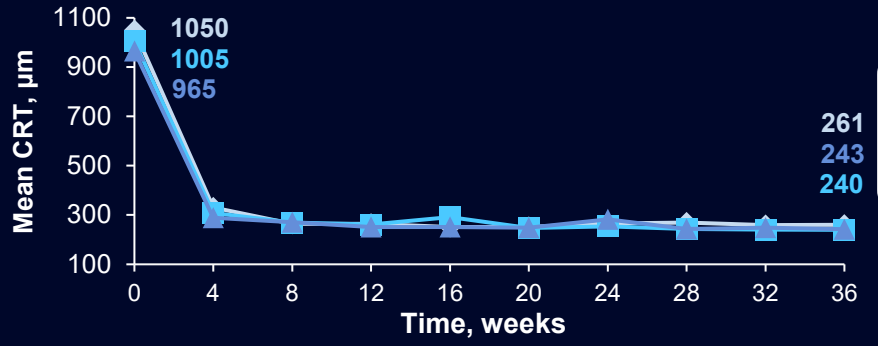
Baseline CRT	BRVO	Mean no. of injections[a]			CRVO/HRVO	Baseline CRT
		BRVO	CRVO/HRVO			
≤452 µm 2q4, n=48 8q8/3, n=53 8q8/5, n=54		8.8 6.0 6.8	8.8 6.0 6.9			≤576 µm 2q4, n=41 8q8/3, n=45 8q8/5, n=55
>452–≤586 µm 2q4, n=55 8q8/3, n=52 8q8/5, n=49		8.8 6.0 7.0	8.6 6.1 6.8			>576–≤798 µm 2q4, n=61 8q8/3, n=43 8q8/5, n=38
>586 µm 2q4, n=46 8q8/3, n=54 8q8/5, n=56		8.8 6.2 7.0	8.8 6.1 7.0			>798 µm 2q4, n=49 8q8/3, n=46 8q8/5, n=46

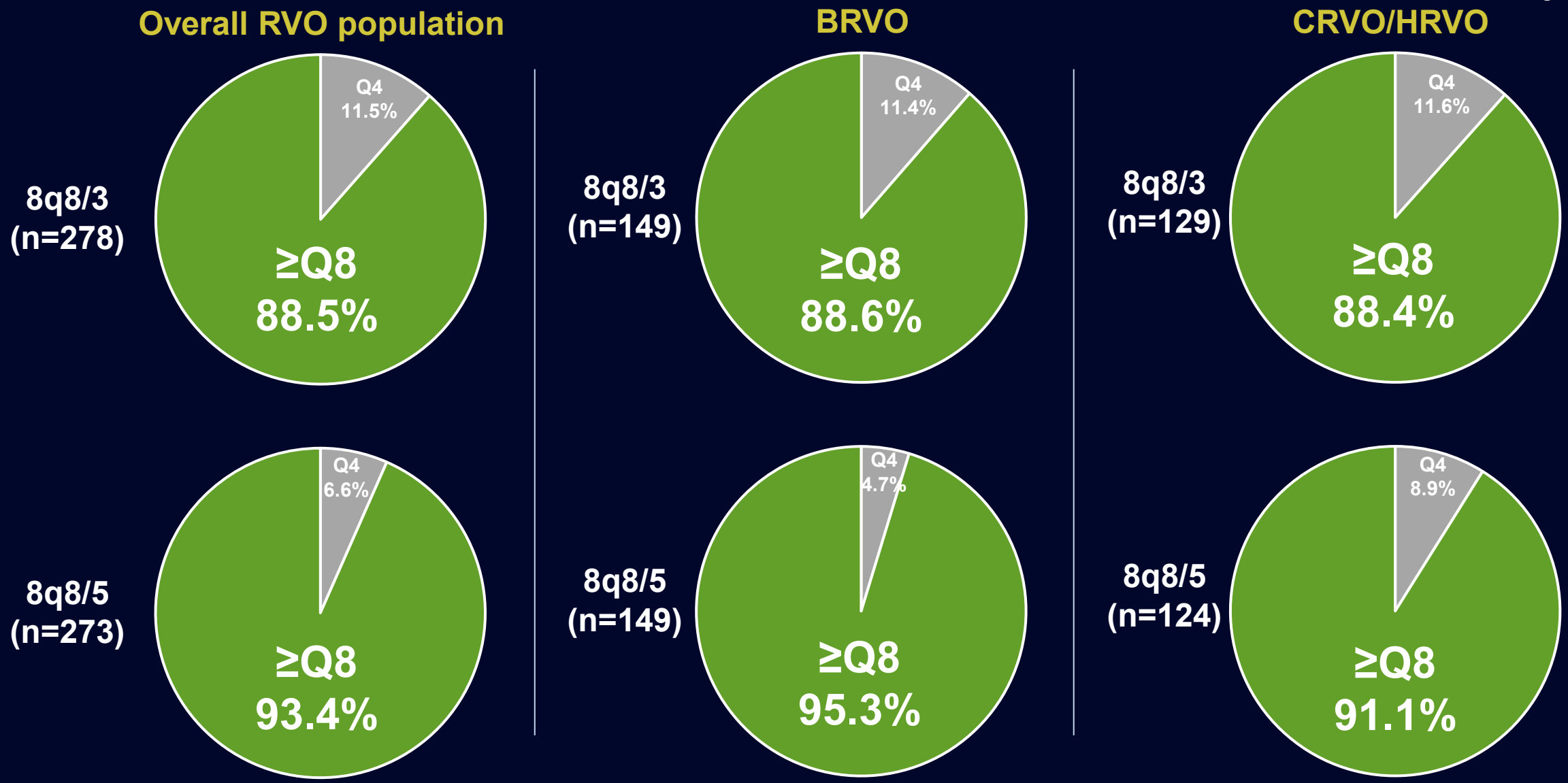
Full analysis set. Observed cases excluding values after intercurrent event: Observations after the occurrence of an intercurrent event are excluded in line with the primary estimand strategy. CRT tertiles for BRVO were ≤452 µm, >452–≤586 µm, and >586 µm and for CRVO/HRVO were ≤576 µm, >576–≤798 µm, and >798 µm. [a]Safety analysis set. Patients completing Week 36.

Robust CRT Improvements Achieved Across Treatment Groups, with Fewer Injections Across Baseline CRT Tertiles by RVO Subtypes

Baseline CRT	BRVO	Mean no. of injections[a]		CRVO/HRVO	Baseline CRT
		BRVO	CRVO/HRVO		
≤452 µm 2q4, n=48 8q8/3, n=53 8q8/5, n=54		8.8 6.0 6.8	8.8 6.0 6.9		≤576 µm 2q4, n=41 8q8/3, n=45 8q8/5, n=55
>452–≤586 µm 2q4, n=55 8q8/3, n=52 8q8/5, n=49		8.8 6.0 7.0	8.6 6.1 6.8		>576–≤798 µm 2q4, n=61 8q8/3, n=43 8q8/5, n=38
>586 µm 2q4, n=46 8q8/3, n=54 8q8/5, n=56		8.8 6.2 7.0	8.8 6.1 7.0		>798 µm 2q4, n=49 8q8/3, n=46 8q8/5, n=46

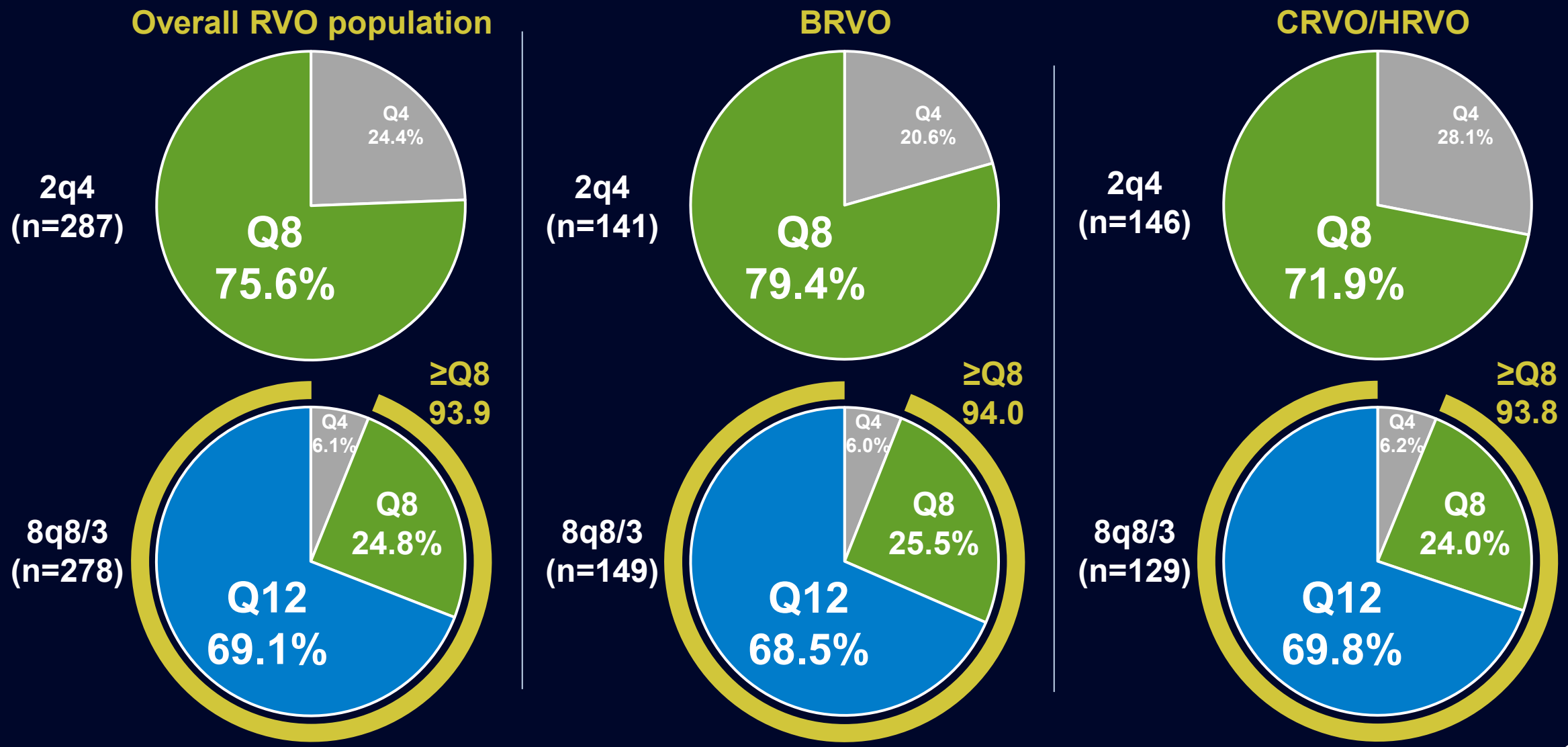
Full analysis set. Observed cases excluding values after intercurrent event: Observations after the occurrence of an intercurrent event are excluded in line with the primary estimand strategy. CRT tertiles for BRVO were ≤452 µm, >452–≤586 µm, and >586 µm and for CRVO/HRVO were ≤576 µm, >576–≤798 µm, and >798 µm. [a]Safety analysis set. Patients completing Week 36.

Most Patients in the Aflibercept 8 mg Groups Maintained ≥Q8 Dosing Intervals through Week 36



Safety analysis set. Patients completing Week 36. **Q4**, every 4 weeks; **Q8**, every 8 weeks.

Most Patients Eligible for Dosing Interval Extension Treated with Aflibercept 8 mg Were Last Assigned to ≥Q8 Dosing Intervals at Week 36



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

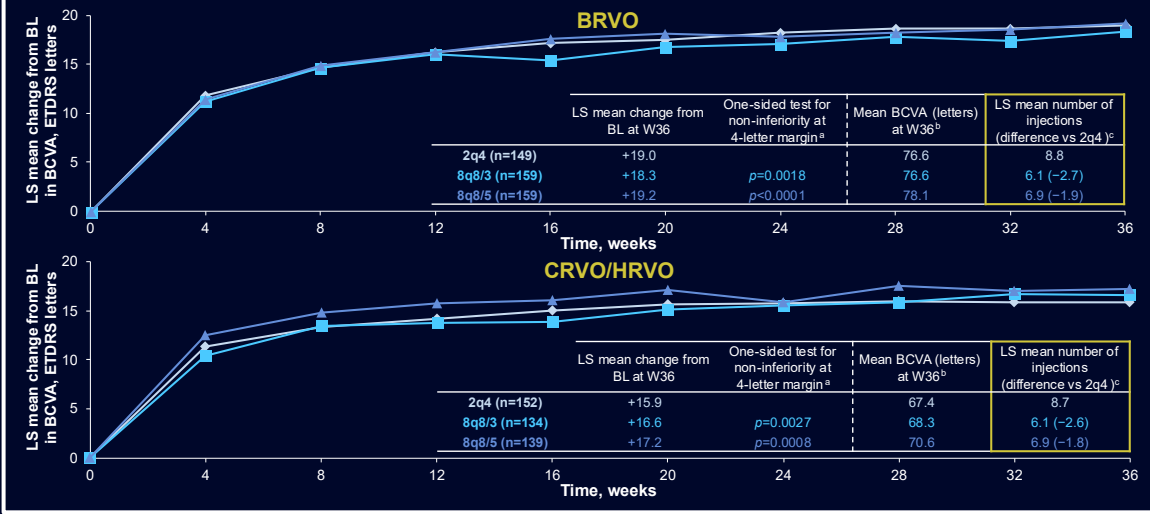
Aflibercept 8 mg had a safety profile consistent with the established safety profile of aflibercept 2 mg and 8 mg

Safety analysis set. IOI-related events of anterior chamber cell and iritis were considered mild, the events of eye inflammation, uveitis, and endophthalmitis (2q4 group, n=2) were considered moderate; the case of endophthalmitis in the 8q8/3 group was considered severe. Endophthalmitis events were considered serious and injection-procedure-related; 1 event (2q4 group) was considered intervention-related. The event of eye inflammation was considered intervention-related. No IOI-related events resulted in discontinuation of study intervention. **APTC**, Anti-Platelet Trialists' Collaboration; **IOI**, intraocular inflammation; **SAE**, serious adverse event; **TEAE**, treatment-emergent adverse event.

QUASAR: Both Aflibercept 8 mg Groups Achieved Visual and Anatomic Improvements with Fewer Injections Than 2q4

- Aflibercept 8q8/3 and 8q8/5 groups achieved **non-inferior BCVA gains and robust reductions in CRT** at Week 36 with fewer injections than in the aflibercept 2q4 group, and consistent results across BRVO and CRVO/HRVO subtypes
- **Mean BCVA gains and CRT improvements were similar across baseline CRT tertiles with fewer injections** after treatment with aflibercept 8 mg compared with aflibercept 2 mg across BRVO and CRVO/HRVO subtypes
- Approximately **94% of patients across both RVO subtypes in the aflibercept 8q8/3 group were last assigned to ≥8-week dosing intervals at Week 36**
- 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 BCVA Gains Compared to 2q4 at Week 36, with Fewer Injections Across RVO Subtypes



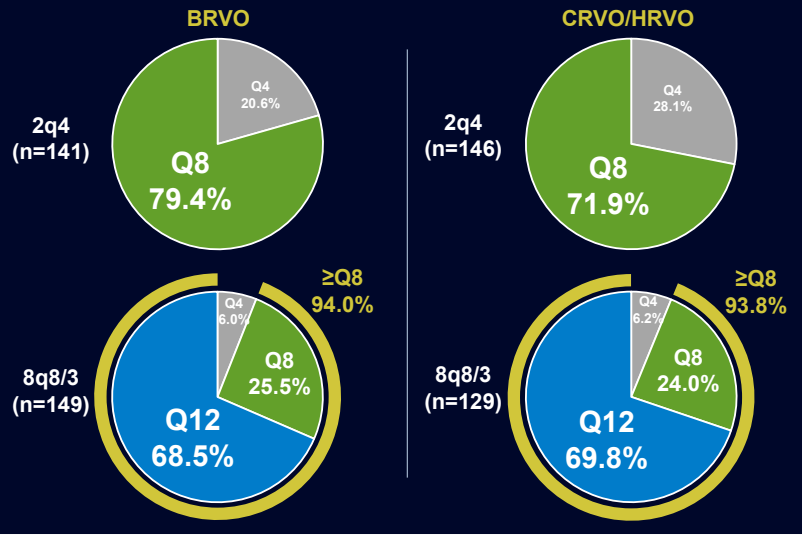
BRVO

	LS mean change from BL at W36	One-sided test for non-inferiority at 4-letter margin[a]	Mean BCVA (letters) at W36[b]	LS mean number of injections (difference vs 2q4)[c]
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	One-sided test for non-inferiority at 4-letter margin[a]	Mean BCVA (letters) at W36[b]	LS mean number of injections (difference vs 2q4)[c]
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)

Last Assigned Dosing Interval at Week 36 for Patients Eligible for Interval Extension Across RVO Subtypes[d]



Full analysis set. [a]Observed values (censoring data post intercurrent event). [b]Missing endpoint values imputed using a multiple imputation procedure. [c]Nominal *p*-values. [d]Safety 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.