



**Impact of Baseline Central Retinal Thickness on Visual and
Anatomic Outcomes in Patients With Macular Edema Following
Retinal Vein Occlusion: Post Hoc Analysis of the
Phase 3 QUASAR Trial Through Week 36**

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Background and Objective

- The phase 3 QUASAR trial met its primary endpoint, with aflibercept 8 mg achieving noninferior gains in BCVA and a robust reduction in CRT comparable to aflibercept 2 mg through Week 36¹
- Understanding baseline factors associated with visual and anatomic outcomes can help treatment decisions and facilitate appropriate physician and patient expectations

This post hoc analysis evaluated the impact of baseline CRT on visual and anatomic outcomes in patients with macular edema following RVO treated with aflibercept 8 mg versus aflibercept 2 mg in QUASAR

QUASAR Study Design



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

2q4

Aflibercept 2 mg every 4 weeks
n=301

8q8/3

Aflibercept 8 mg every 8 weeks
after 3 initial monthly injections
n=293

8q8/5

Aflibercept 8 mg every 8 weeks
after 5 initial monthly injections
n=298

Primary endpoint at Week 36
Change from baseline in BCVA (noninferiority)

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



End of study at Week 64

QUASAR Dosing Regimen

	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 ^b	T&E
8q8/3	X	X	X	o	X ^a	o	X ^a	o	X ^{a,b}	T&E
8q8/5	X	X	X	X	X	o	X ^a	o	X ^a	o

□ Indicates reference visit for DRM assessment (Week 12 for 8q8/3 and Week 20 for 2q4 and 8q8/5)

▲ Primary endpoint
Mean change in
BCVA (noninferiority)

^aDRM: Interval Shortening

- Patients in the 8q8/3, 8q8/5, and 2q4 groups could qualify for interval shortening at a dosing visit beginning at Weeks 16, 24, and 40, respectively
- Criteria for interval shortening:**
 - >5-letter loss in BCVA from reference visit^c
 - AND
 - >50-μm increase in CRT from reference visit^c
- Dosing intervals were shortened by 4-week increments if patients met the DRM criteria and their last dosing interval was ≥Q8

^bDRM: Interval Extension

- Patients in the 2q4 and 8q8/3 groups could qualify for interval extension at a dosing visit beginning at Week 32 and those in 8q8/5 qualified at Week 40
- Criteria for interval extension:**
 - <5-letter loss in BCVA from reference visit^c
 - AND
 - CRT <320 μm on Heidelberg Spectralis (<300 μm on Cirrus or Topcon SD-OCT)
- Dosing intervals were extended by 4-week increments if DRM criteria were met

Stippled boxes = initial treatment phase; X = active injection; o = sham injection. Figure does not reflect all dosing options if the intervals are shortened.

^cReference visit defined as Week 12 for 8q8/3 and Week 20 for 8q8/5 and 2q4.

DRM, dose regimen modification; Q8, every 8 weeks; SD-OCT, spectral domain-optical coherence tomography; T&E, treat and extend; Wk, week.

Methods

- A tertile analysis by baseline CRT was conducted post hoc to evaluate visual and anatomic outcomes through Week 36 following treatment with aflibercept 8 mg and 2 mg in patients from QUASAR
- Data through Week 36 for the full analysis were evaluated by RVO subtype (BRVO or CRVO/HRVO). Patients were grouped by baseline CRT as follows:

BRVO

T1: $\leq 452 \mu\text{m}$	T2: $>452 \text{ to } \leq 586 \mu\text{m}$	T3: $>586 \mu\text{m}$
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CRVO/HRVO

T1: $\leq 576 \mu\text{m}$	T2: $>576 \text{ to } \leq 798 \mu\text{m}$	T3: $>798 \mu\text{m}$
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- Outcomes were summarized descriptively

Baseline Characteristics of Patients With BRVO by Baseline CRT

	T1: ≤452 μm			T2: >452 to ≤586 μm			T3: >586 μm		
	2q4 (n=48)	8q8/3 (n=53)	8q8/5 (n=54)	2q4 (n=55)	8q8/3 (n=52)	8q8/5 (n=49)	2q4 (n=46)	8q8/3 (n=54)	8q8/5 (n=56)
Age, mean (SD), years	63.0 (11.4)	64.9 (10.6)	66.0 (12.6)	66.6 (9.0)	65.9 (10.1)	64.5 (12.4)	64.9 (11.8)	64.7 (11.6)	64.5 (9.5)
Female, n (%)	31 (64.6)	31 (58.5)	30 (55.6)	28 (50.9)	21 (40.4)	26 (53.1)	19 (41.3)	31 (57.4)	31 (55.4)
Race, n (%)									
White	26 (54.2)	31 (58.5)	27 (50.0)	28 (50.9)	31 (59.6)	28 (57.1)	27 (58.7)	25 (46.3)	30 (53.6)
Asian	20 (41.7)	17 (32.1)	23 (42.6)	24 (43.6)	16 (30.8)	16 (32.7)	17 (37.0)	24 (44.4)	24 (42.9)
Other ^a	2 (4.2)	5 (9.4)	4 (7.4)	3 (5.5)	5 (9.6)	5 (10.2)	2 (4.3)	5 (9.3)	2 (3.6)
Hispanic or Latino, n (%)	5 (10.4)	4 (7.5)	3 (5.6)	1 (1.8)	3 (5.8)	2 (4.1)	5 (10.9)	4 (7.4)	3 (5.4)
BCVA, mean (SD), ETDRS letters	63.7 (9.3)	63.7 (9.7)	61.9 (9.6)	59.0 (11.0)	57.8 (10.8)	62.5 (8.7)	48.5 (14.5)	54.4 (11.9)	51.9 (12.4)
CRT, mean (SD), μm	381.2 (43.6)	377.6 (48.8)	386.2 (47.6)	532.3 (41.4)	520.6 (39.9)	511.8 (42.7)	755.9 (129.0)	744.0 (116.4)	714.8 (126.4)
Total area of macular ischemia,^b mean (SD), mm²	4.5 (3.6)	3.8 (3.3)	4.6 (3.5)	6.1 (3.7)	6.7 (3.2)	5.9 (4.0)	7.5 (3.5)	6.6 (4.0)	7.8 (3.9)

Patients with BRVO in the FAS.

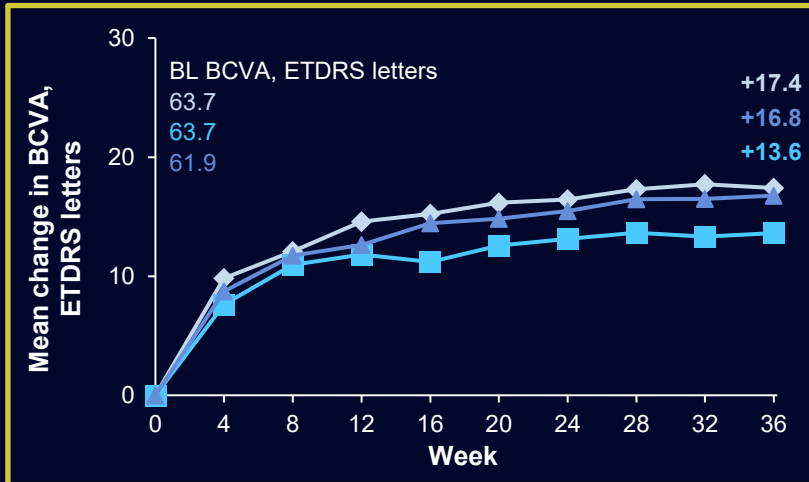
^aOther includes Black or African American, Native Hawaiian or other Pacific Islander, Not reported, and Multiple categories.

^bMacular ischemia was evaluated by FA; foveal avascular zone was not considered.

ETDRS, Early Treatment Diabetic Retinopathy Study; FA, fluorescein angiography; FAS, full analysis set.

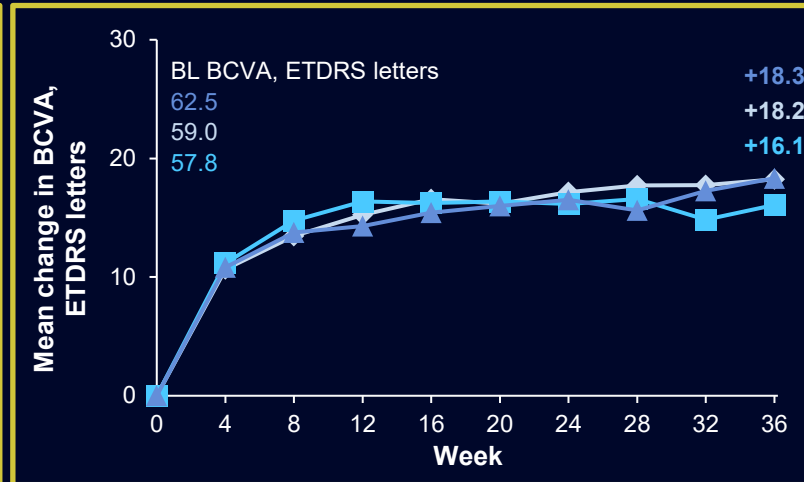
Mean Change in BCVA Through Week 36 by Baseline CRT in Patients With BRVO

T1: $\leq 452 \mu\text{m}$



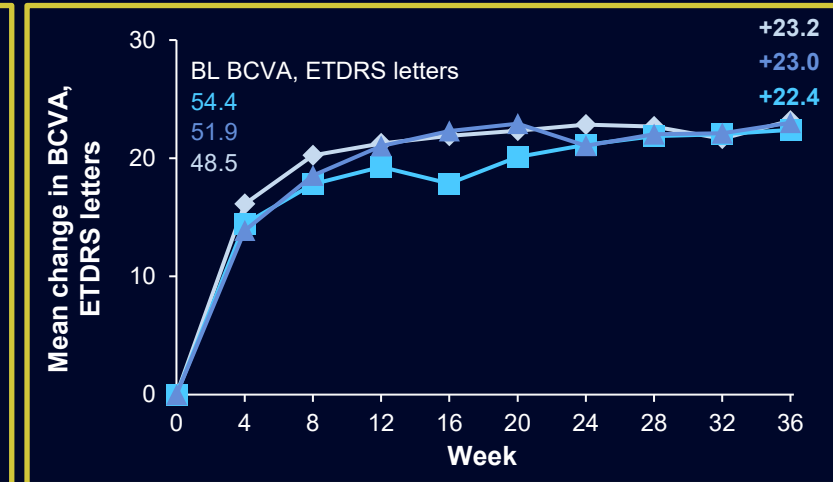
Mean number of injections ^a	
2q4 (n=48)	8.8
8q8/3 (n=53)	6.0
8q8/5 (n=54)	6.8

T2: >452 to $\leq 586 \mu\text{m}$



Mean number of injections ^a	
2q4 (n=55)	8.8
8q8/3 (n=52)	6.0
8q8/5 (n=49)	7.0

T3: $>586 \mu\text{m}$



Mean number of injections ^a	
2q4 (n=46)	8.8
8q8/3 (n=54)	6.2
8q8/5 (n=56)	7.0

In BRVO, aflibercept 8 mg achieved robust improvements in BCVA through Week 36, with fewer injections than aflibercept 2 mg across all baseline CRT tertiles

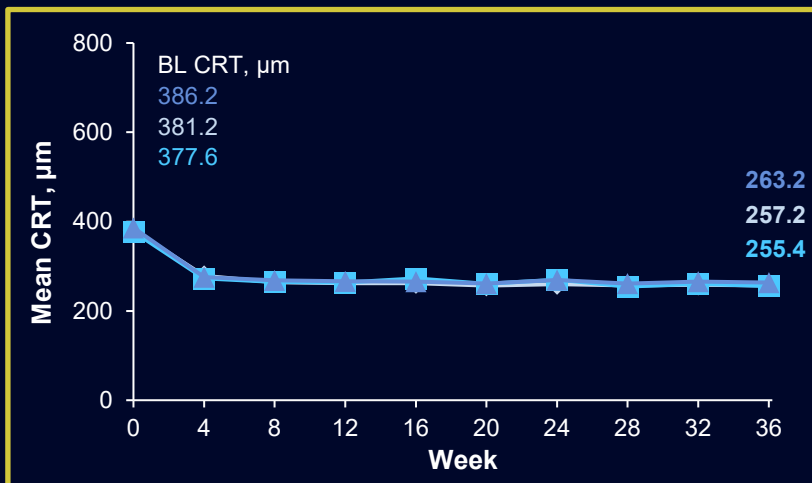
Patients with BRVO in the FAS, observed cases excluding intercurrent events.

^aPatients who completed the Week 36 visit.

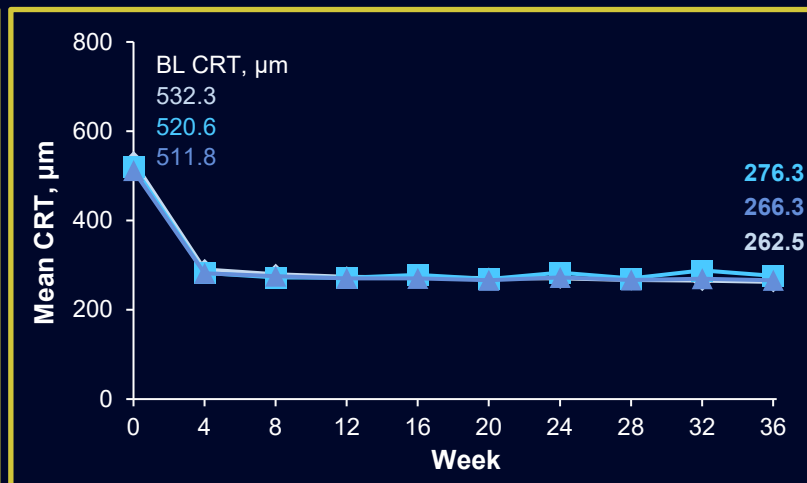
BL, baseline.

Mean CRT Through Week 36 by Baseline CRT in Patients With BRVO

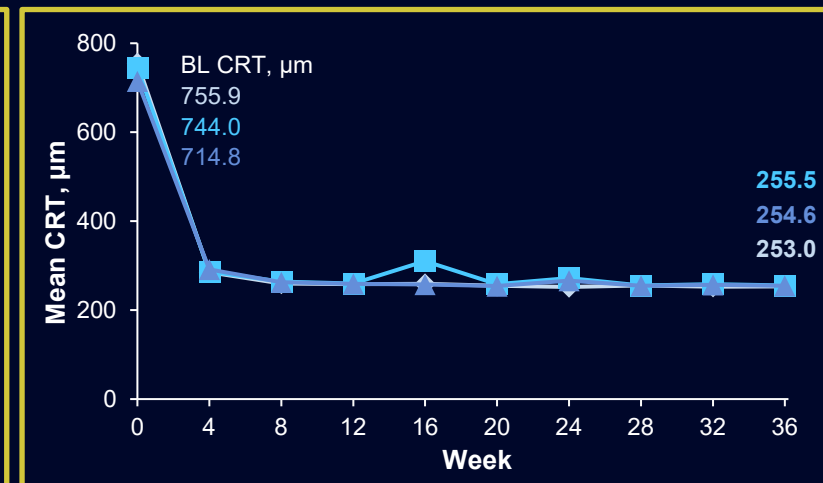
T1: $\leq 452 \mu\text{m}$



T2: >452 to $\leq 586 \mu\text{m}$



T3: $>586 \mu\text{m}$



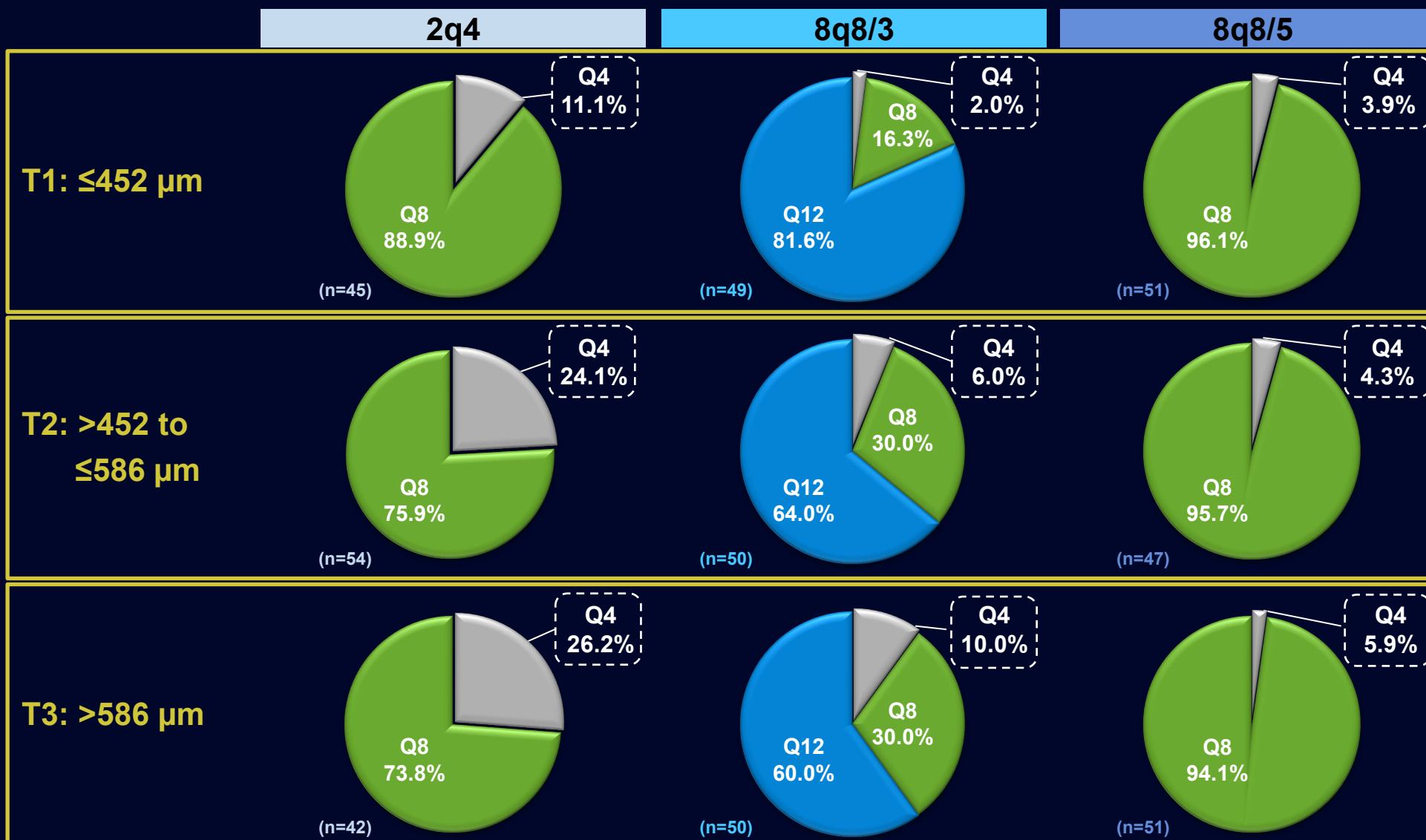
Mean number of injections ^a	
2q4 (n=48)	8.8
8q8/3 (n=53)	6.0
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Mean number of injections ^a	
2q4 (n=55)	8.8
8q8/3 (n=52)	6.0
8q8/5 (n=49)	7.0

Mean number of injections ^a	
2q4 (n=46)	8.8
8q8/3 (n=54)	6.2
8q8/5 (n=56)	7.0

In BRVO, aflibercept 8 mg achieved robust CRT reduction through Week 36, with fewer injections than aflibercept 2 mg across all baseline CRT tertiles

Last Assigned Dosing Interval at Week 36 by Baseline CRT in Patients With BRVO



8q8/5 group:
Per DRM criteria,
patients could not
qualify for dosing
interval extension
until Week 40

Baseline Characteristics of Patients With CRVO/HRVO by Baseline CRT

	T1: ≤576 μm			T2: >576 to ≤798 μm			T3: >798 μm		
	2q4 (n=41)	8q8/3 (n=45)	8q8/5 (n=55)	2q4 (n=61)	8q8/3 (n=43)	8q8/5 (n=38)	2q4 (n=49)	8q8/3 (n=46)	8q8/5 (n=46)
Age, mean (SD), years	67.8 (12.4)	66.1 (11.7)	65.2 (11.4)	69.3 (10.4)	66.5 (13.0)	68.8 (13.0)	63.5 (14.5)	67.3 (12.8)	66.9 (10.0)
Female, n (%)	17 (41.5)	17 (37.8)	23 (41.8)	27 (44.3)	18 (41.9)	15 (39.5)	21 (42.9)	18 (39.1)	21 (45.7)
Race, n (%)									
White	29 (70.7)	34 (75.6)	37 (67.3)	36 (59.0)	26 (60.5)	24 (63.2)	32 (65.3)	26 (56.5)	31 (67.4)
Asian	10 (24.4)	8 (17.8)	14 (25.5)	16 (26.2)	12 (27.9)	9 (23.7)	13 (26.5)	14 (30.4)	11 (23.9)
Other ^a	2 (4.9)	3 (6.7)	4 (7.3)	9 (14.8)	5 (11.6)	5 (13.2)	4 (8.2)	6 (13.0)	4 (8.7)
Hispanic or Latino, n (%)	2 (4.9)	4 (8.9)	2 (3.6)	5 (8.2)	4 (9.3)	3 (7.9)	4 (8.2)	6 (13.0)	1 (2.2)
BCVA, mean (SD), ETDRS letters	60.8 (10.1)	58.6 (12.3)	58.2 (13.0)	54.1 (10.9)	54.3 (14.3)	53.9 (11.8)	39.4 (14.3)	41.4 (12.1)	42.5 (13.8)
CRT, mean (SD), μm	467.1 (80.0)	461.6 (81.2)	455.0 (72.9)	694.2 (57.3)	678.5 (58.5)	689.1 (68.9)	1050.0 (191.9)	1005.5 (185.8)	964.8 (135.2)
Total area of macular ischemia, ^b mean (SD), mm ²	2.2 (3.6)	4.2 (6.3)	3.5 (5.2)	1.1 (2.4)	2.6 (4.1)	1.3 (3.2)	4.8 (7.8)	4.1 (6.4)	3.8 (6.8)

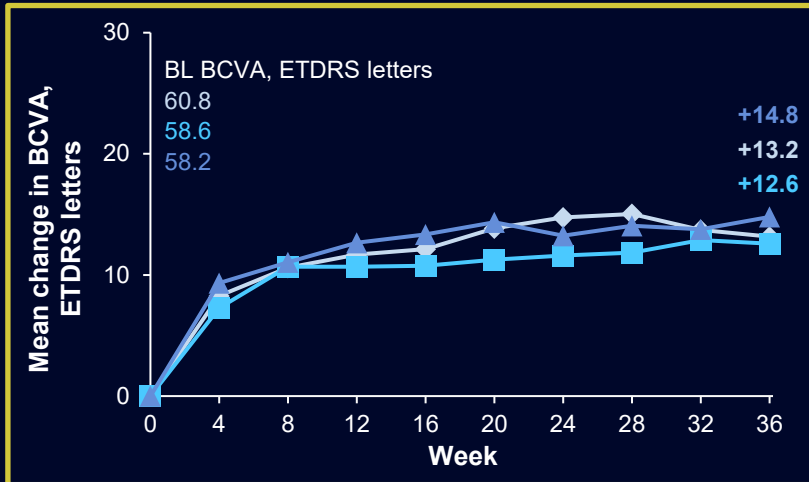
Patients with CRVO/HRVO in the FAS.

^aOther includes Black or African American, American Indian or Alaska Native, Not reported, and Multiple categories.

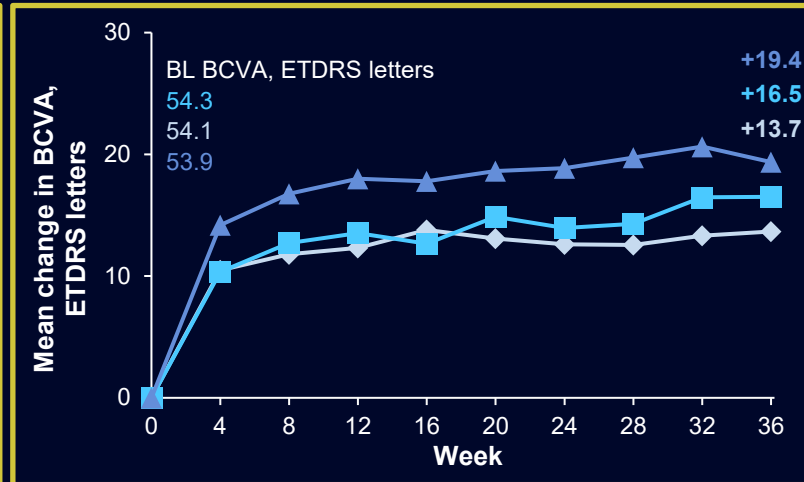
^bMacular ischemia was evaluated by FA; foveal avascular zone was not considered.

Mean Change in BCVA Through Week 36 by Baseline CRT in Patients With CRVO/HRVO

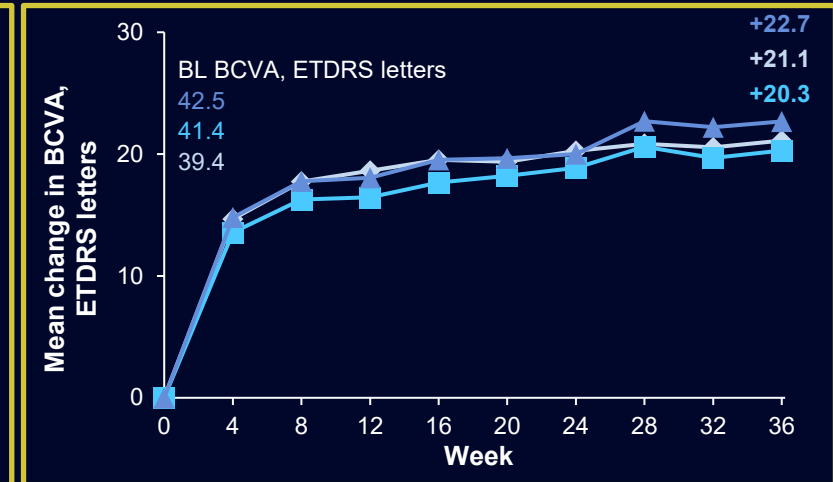
T1: $\leq 576 \mu\text{m}$



T2: >576 to $\leq 798 \mu\text{m}$



T3: $>798 \mu\text{m}$



Mean number of injections ^a	
2q4 (n=41)	8.8
8q8/3 (n=45)	6.0
8q8/5 (n=55)	6.9

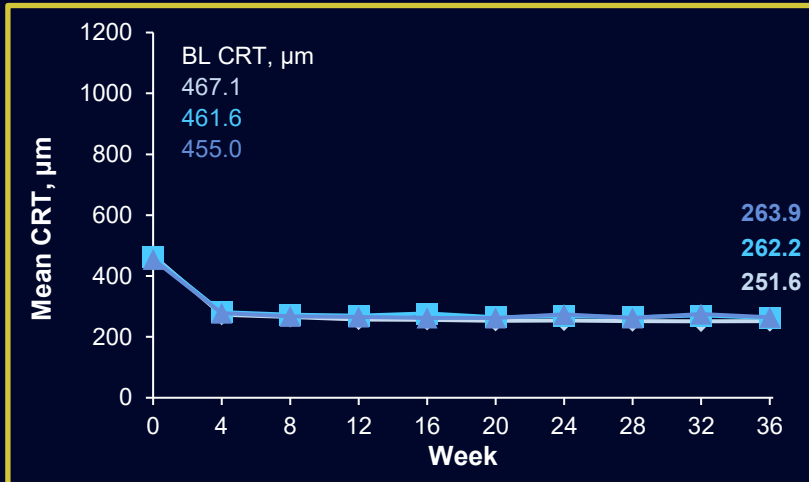
Mean number of injections ^a	
2q4 (n=61)	8.6
8q8/3 (n=43)	6.1
8q8/5 (n=38)	6.8

Mean number of injections ^a	
2q4 (n=49)	8.8
8q8/3 (n=46)	6.1
8q8/5 (n=46)	7.0

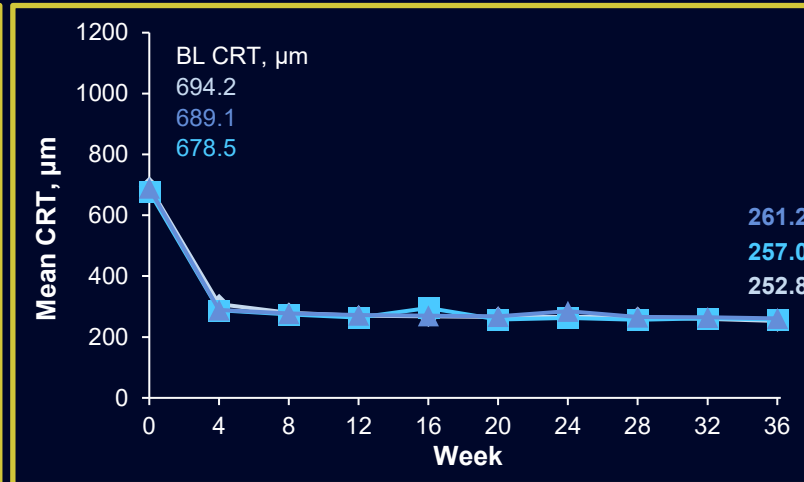
In CRVO/HRVO, aflibercept 8 mg achieved robust improvements in BCVA through Week 36, with fewer injections than aflibercept 2 mg across all baseline CRT tertiles

Mean CRT Through Week 36 by Baseline CRT in Patients With CRVO/HRVO

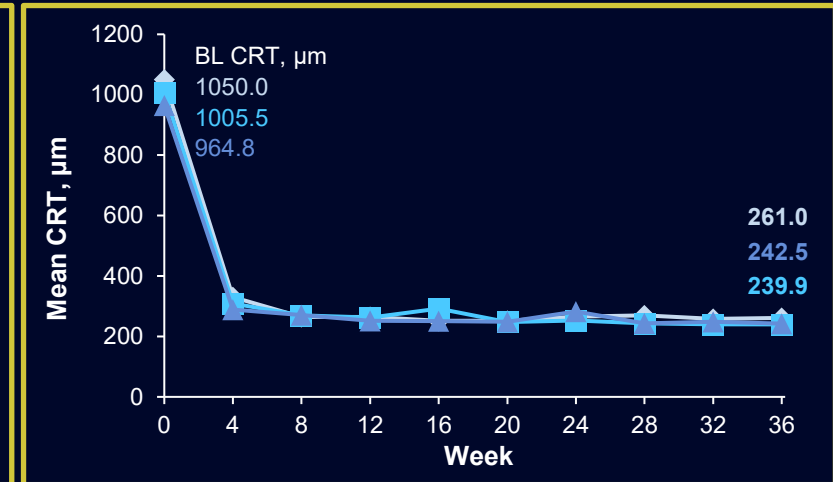
T1: ≤576 μm



T2: >576 to ≤798 μm



T3: >798 μm



Mean number of injections^a

2q4 (n=41)	8.8
8q8/3 (n=45)	6.0
8q8/5 (n=55)	6.9

Mean number of injections^a

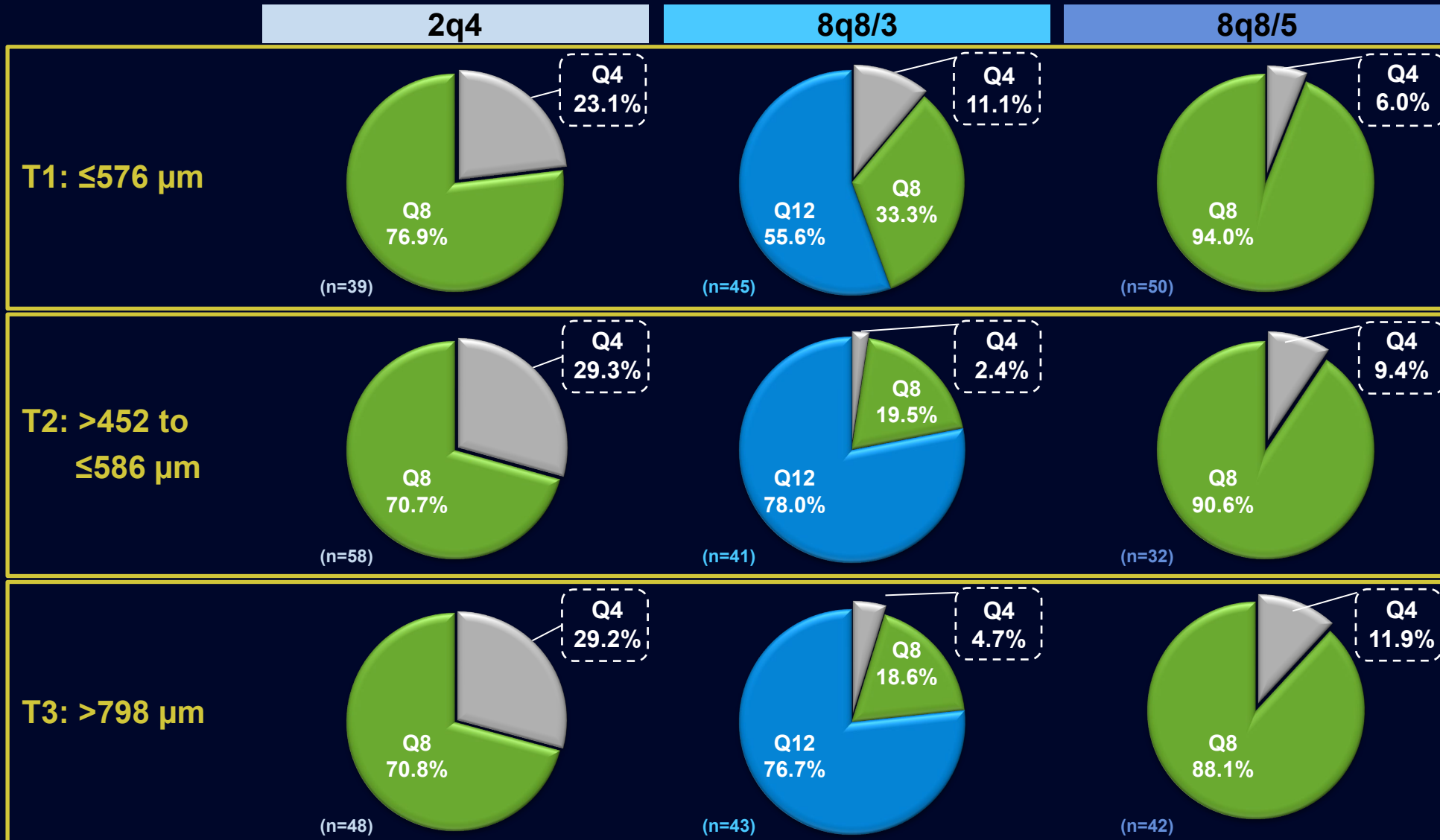
2q4 (n=61)	8.6
8q8/3 (n=43)	6.1
8q8/5 (n=38)	6.8

Mean number of injections^a

2q4 (n=49)	8.8
8q8/3 (n=46)	6.1
8q8/5 (n=46)	7.0

In CRVO/HRVO, aflibercept 8 mg achieved robust CRT reduction through Week 36, with fewer injections than aflibercept 2 mg across all baseline CRT tertiles

Last Assigned Dosing Interval at Week 36 by Baseline CRT in Patients With CRVO/HRVO



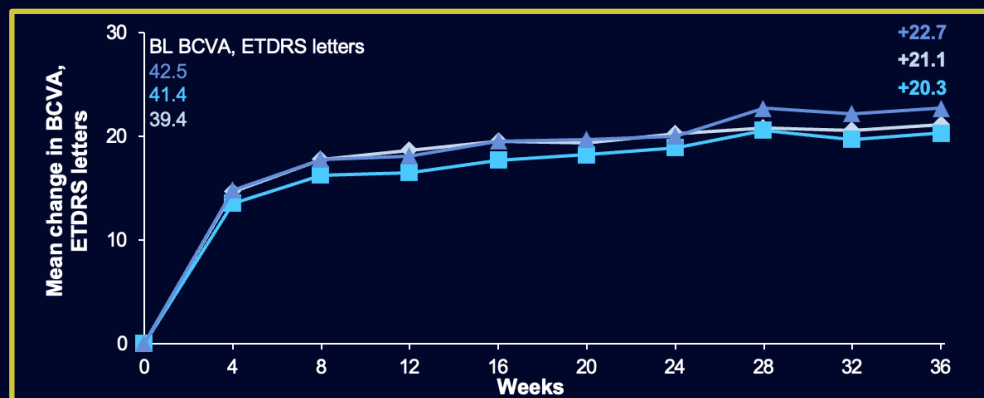
8q8/5 group:
Per DRM criteria,
patients could not
qualify for dosing
interval extension
until Week 40

Conclusions

- Aflibercept 8 mg achieved robust visual and anatomic improvements through Week 36 in patients with macular edema following RVO across all baseline CRT tertiles with fewer injections compared with aflibercept 2 mg
- Substantially fewer patients required Q4 dosing with aflibercept 8 mg compared with 2 mg at Week 36 regardless of baseline CRT tertile and RVO type

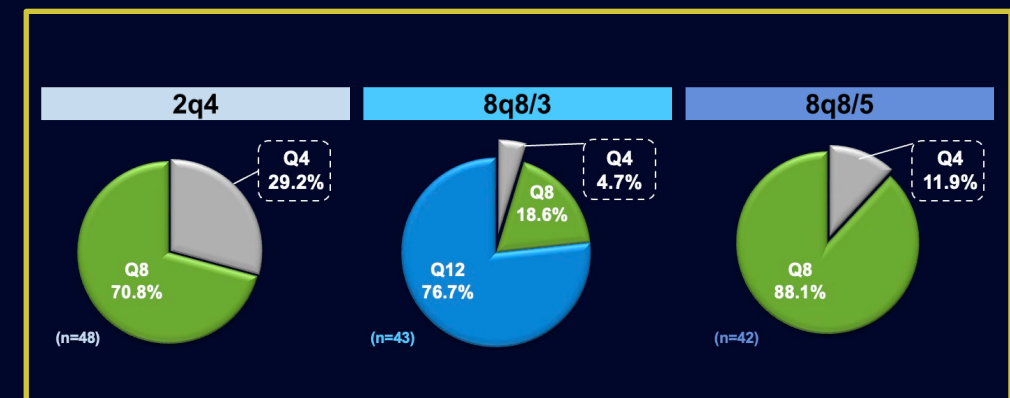
**Mean Change in BCVA Through Week 36
by Baseline CRT^a**
T3: >798 μ m

CRVO/
HRVO



**Last Assigned Dosing Interval at Week 36
by Baseline CRT^b**
T3: >798 μ m

CRVO/
HRVO



^aPatients with CRVO/HRVO in the FAS, observed cases excluding intercurrent events.

^bPatients with CRVO/HRVO in the FAS who completed the Week 36 visit. Values may not add up to 100% because of rounding.