



Key Baseline Disease Characteristics in nAMD Are Not Linked to Treatment Interval Extension of Aflibercept 8 mg: A Post hoc PULSAR Analysis

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Disclosures

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PULSAR: Multicenter, Randomized, Double-masked Study¹



Patients with treatment-naïve nAMD were randomly assigned 1:1:1 to receive aflibercept 8q12 (n=335), 8q16 (n=338), or 2q8 (n=336), each after 3 monthly injections

At Week 48, aflibercept 8 mg demonstrated non-inferior BCVA gains with extended dosing intervals versus aflibercept 2 mg in patients with nAMD,¹ with no new safety signals

	YEAR 1													YEAR 2											
	Day 1	W4	W8	W12	W16	W20	W24	W28	W32	W36	W40	W44	W48	W52	W56	W60	W64	W68	W72	W76	W80	W84	W88	W92	W96
2q8	X	X	X		X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	-
8q12	X	X	X		o ^a	X ^a	o	o	X ^a	o	o	X ^a	o	o	X ^{a,b}	o	o	X ^{a,b}	o	o	X ^{a,b}	o	o	X ^{a,b}	-
8q16	X	X	X		o ^a	o ^a	X ^a	o	o	o	X ^a	o	o	o	X ^{a,b}	o	o	o	X ^{a,b}	o	o	o	X ^{a,b}	o	-

Primary endpoint at W48:
Mean change in BCVA (non-inferiority)

End of study at W96
with optional ~1-year extension through W156

^aDRM: Interval shortening during Years 1 and 2

Criteria for interval shortening

- >5-letter loss in BCVA compared with Week 12 due to persistent or worsening nAMD **AND**
- >25 µm increase in CRT compared with Week 12, **OR** new foveal neovascularization, **OR** new foveal hemorrhage

- Patients who met DRM criteria had dosing intervals shortened to q8 at **Weeks 16 and 20** or by 4-week increments from **Week 24**
 - The minimum assigned dosing interval was q8

^bDRM: Interval extension during Year 2

Criteria for interval extension

- <5-letter loss in BCVA compared with Week 12 **AND**
- No fluid at the center subfield on OCT **AND**
- No new foveal hemorrhage or foveal neovascularization

- Patients who met DRM criteria from **Weeks 52 through 96** had dosing intervals extended by 4-week increments
 - The maximum assigned dosing interval was q24

Figure does not reflect all dosing options once a patient's dosing interval is shortened or extended. Stippled boxes = initial treatment phase; X = active injection; o = sham injections. **2q8**, aflibercept 2 mg every 8 weeks; **8q12**, aflibercept 8 mg every 12 weeks; **8q16**, aflibercept 8 mg every 16 weeks; **q8**, every 8 weeks; **q24**, every 24 weeks; **BCVA**, best-corrected visual acuity; **CRT**, central subfield retinal thickness; **DRM**, dose regimen modification; **nAMD**, neovascular age-related macular degeneration; **OCT**, optical coherence tomography; **W**, week. 1. Lanzetta P, et al. *Lancet* 2024;403:1141-1152.

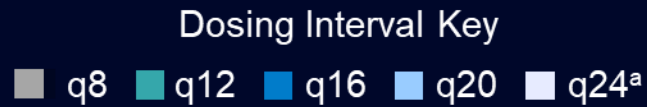
Baseline Demographics and Study Eye Characteristics



	2q8	8q12	8q16	All 8 mg	Total
Randomized, n	336	335	338	673	1009
Age, years	74.2 (8.8)	74.7 (7.9)	74.5 (8.5)	74.6 (8.2)	74.5 (8.4)
Female, %	56.0	54.3	53.3	53.8	54.5
Race, %					
Asian	24.7	22.1	22.8	22.4	23.2
Black or African American	0.6	0.6	0	0.3	0.4
White	74.1	76.4	76.9	76.7	75.8
Not reported	0.6	0.6	0.3	0.4	0.5
Hispanic or Latino, %	3.6	2.1	2.7	2.4	2.8
Hypertension, %	60.7	66.3	64.8	63.9	63.9
BCVA, ETDRS letters	58.9 (14.0)	59.9 (13.4)	60.0 (12.4)	59.9 (12.9)	59.6 (13.3)
CRT, μm	367 (134)	370 (124)	371 (133)	371 (128)	369 (130)
CNV lesion area, mm^2	6.9 (5.4)	6.4 (5.1)	6.9 (5.7)	6.6 (5.4)	6.7 (5.4)

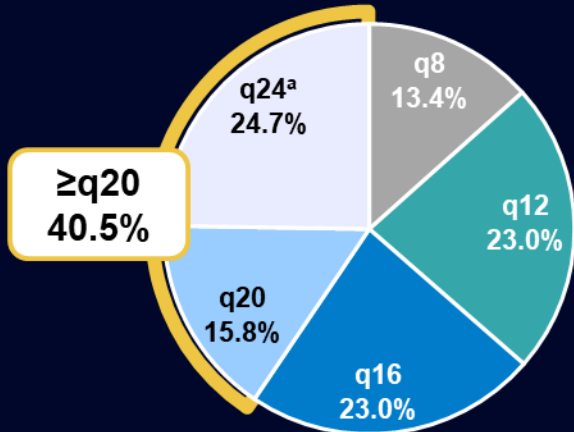
Full analysis set. Data are mean (SD) unless otherwise indicated.
 CNV, choroidal neovascularization; ETDRS, Early Treatment of Diabetic Retinopathy Study; SD, standard deviation.

Last Assigned Dosing Intervals at Week 96 and Objectives of This Analysis

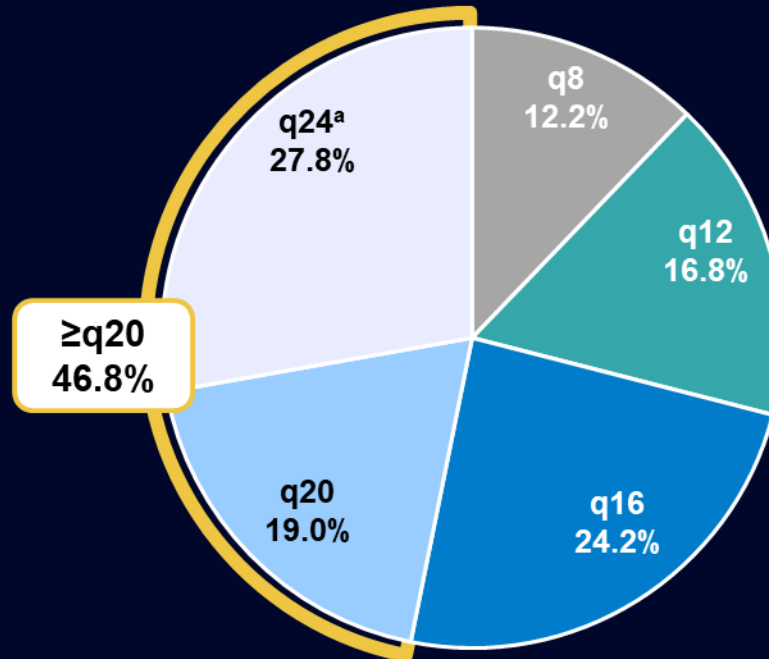
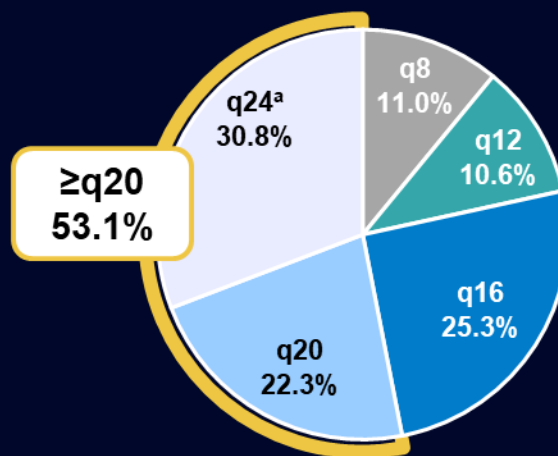


All Patients Receiving 8 mg (n=583)

8q12 (n=291)



8q16 (n=292)



Purpose of this post hoc analysis was to **evaluate baseline characteristics in patients treated with aflibercept 8 mg** in groups defined by dosing intervals in 2 different ways:

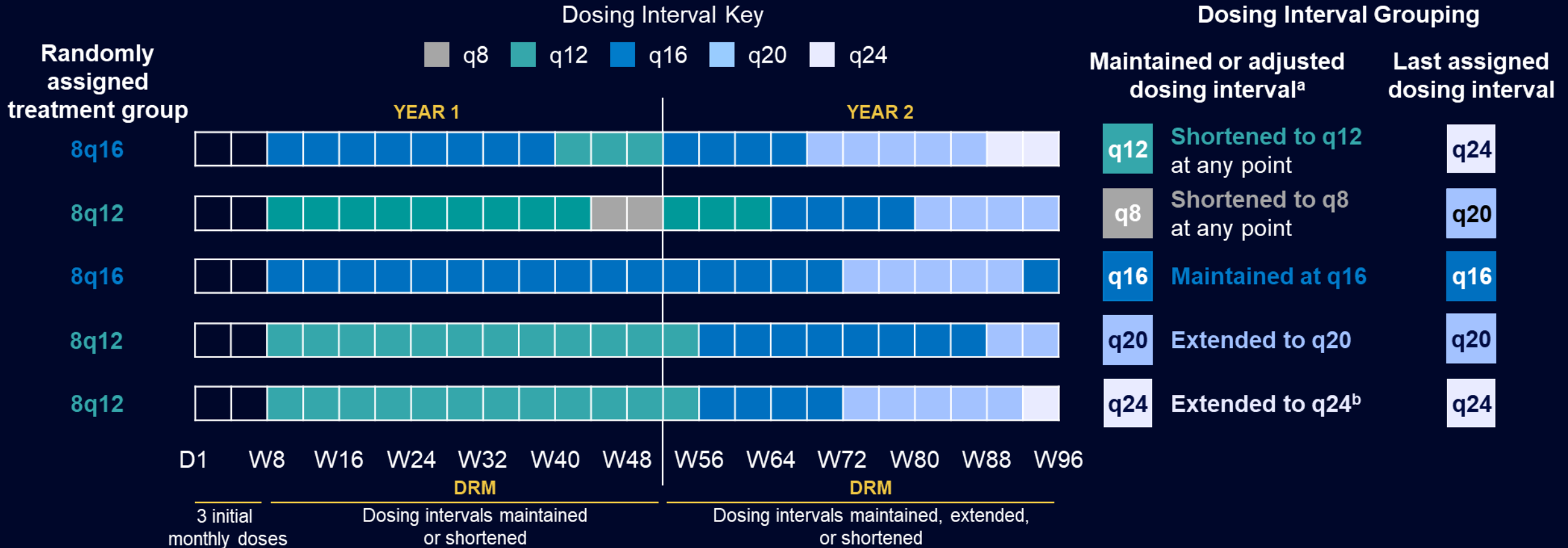
1. According to **whether dosing intervals were shortened, maintained, or extended**
2. According to the **last assigned dosing interval**

Data shown for patients who completed 96 weeks of treatment.

^aPatients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

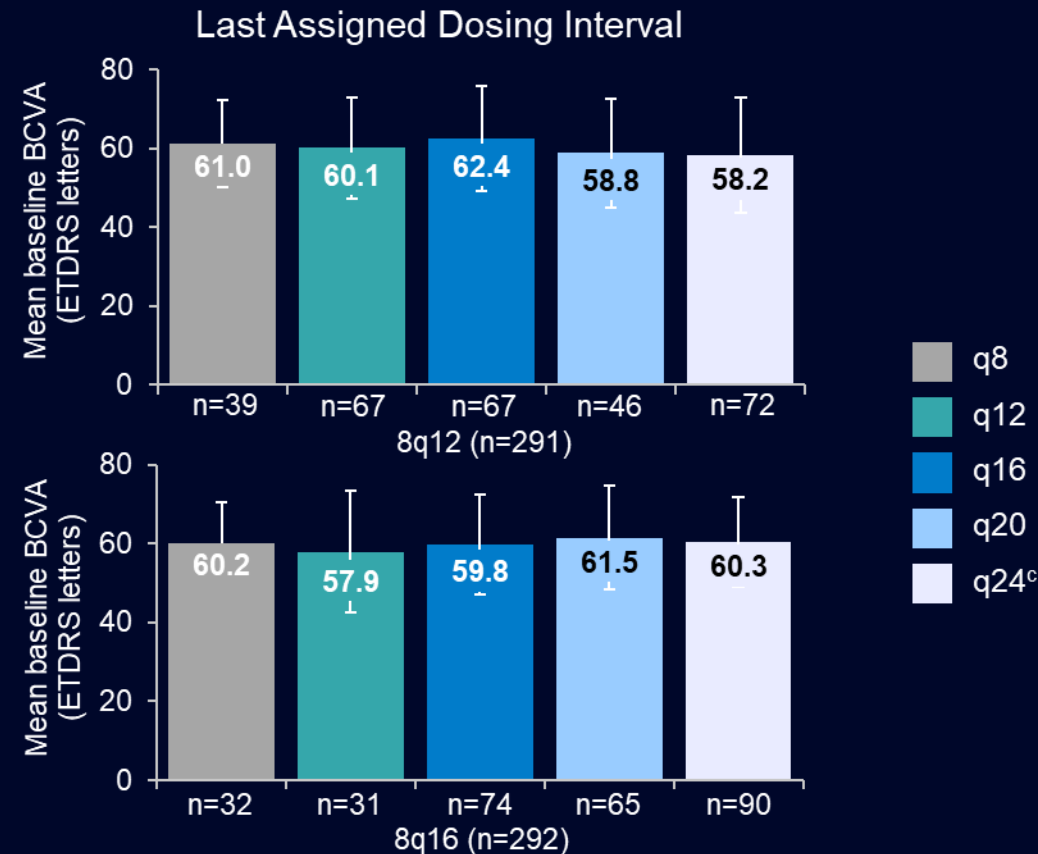
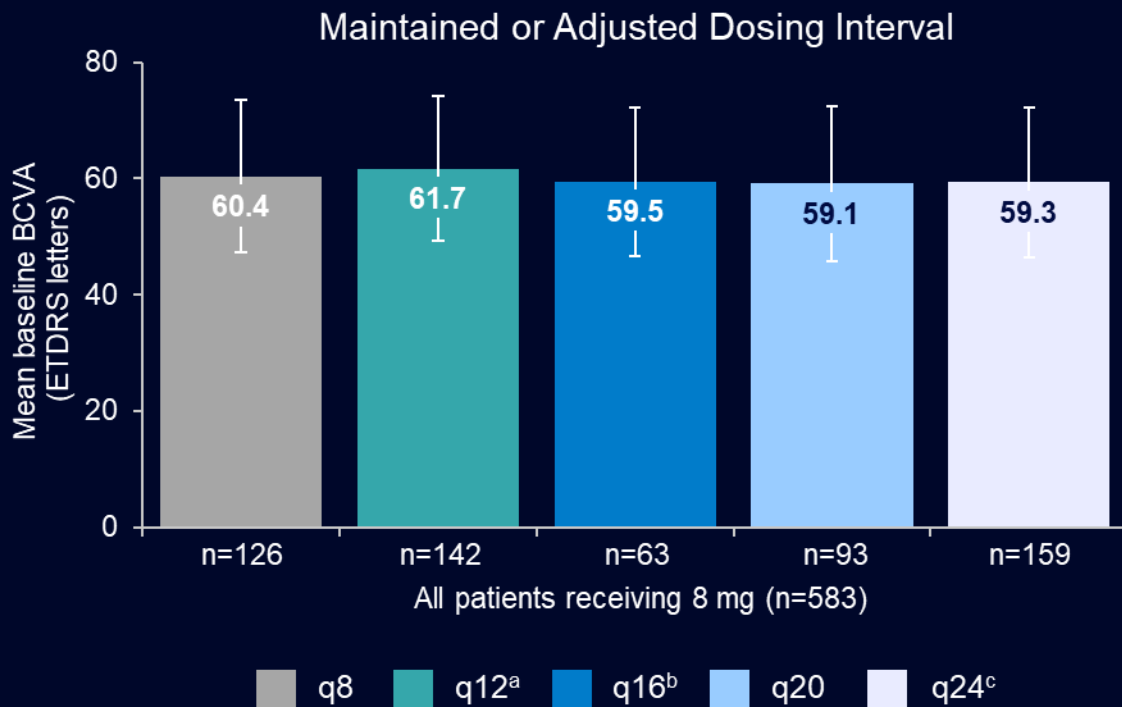
q12, every 12 weeks; q16, every 16 weeks; q20, every 20 weeks.

Understanding Dosing Interval Groupings Through Week 96



^aDefined as the longest dosing interval if the dosing intervals were not shortened throughout the study or the shortest interval if the dosing intervals were shortened at any point throughout the study. ^bPatients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period. D, day.

Baseline BCVA According to Maintained or Adjusted and Last Assigned Dosing Interval Through Week 96

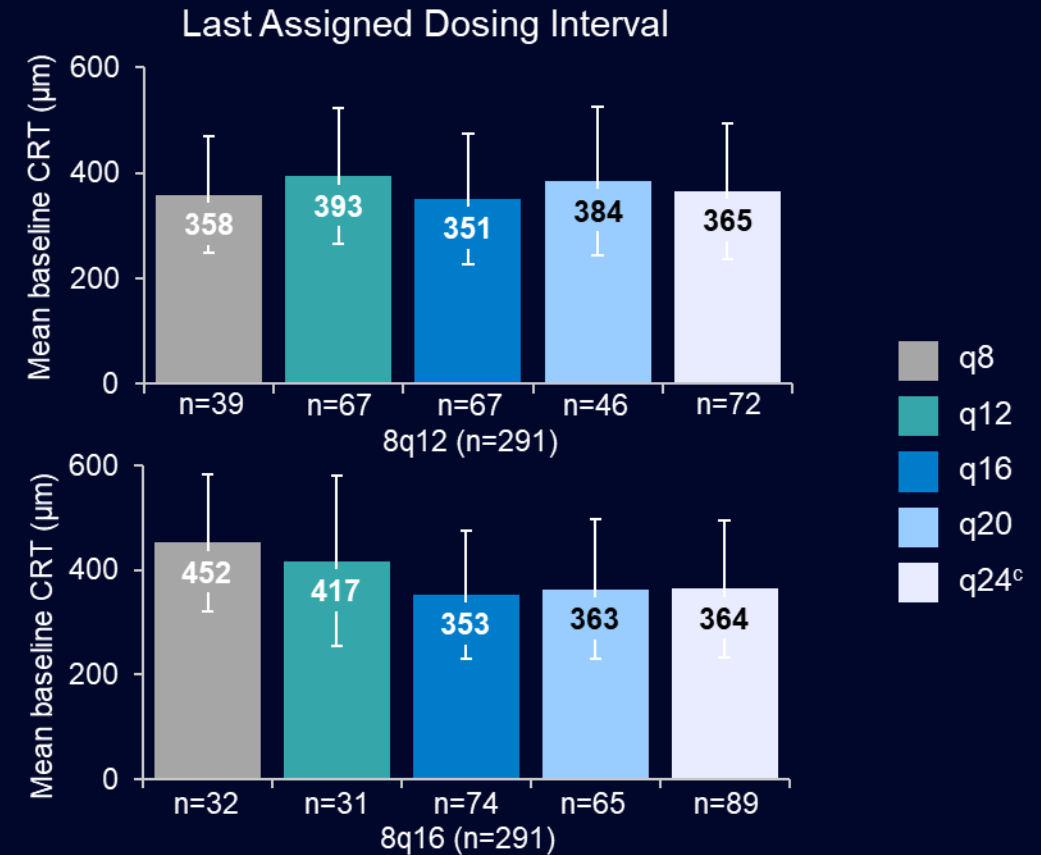
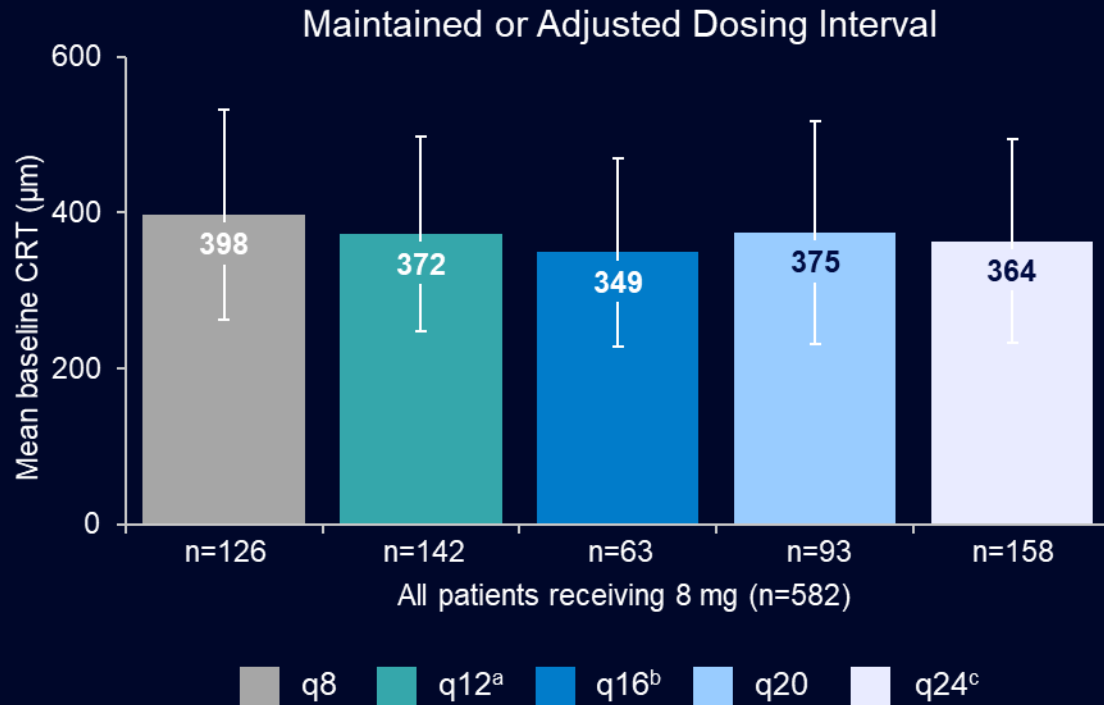


For patients receiving aflibercept 8 mg, **baseline BCVA was similar across groups of patients** as defined by maintained or adjusted dosing interval and according to the last assigned dosing interval at Week 96

Data shown for patients who completed 96 weeks of treatment. Error bars show SD.

^aIncludes patients randomly assigned to 8q12 whose dosing intervals were extended to q16, but not further and includes patients randomly assigned to 8q16 whose dosing intervals were shortened to q12, but not further. ^bIncludes patients randomly assigned to 8q16, whose dosing intervals were not shortened or extended. ^cPatients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

Baseline CRT According to Maintained or Adjusted and Last Assigned Dosing Interval Through Week 96

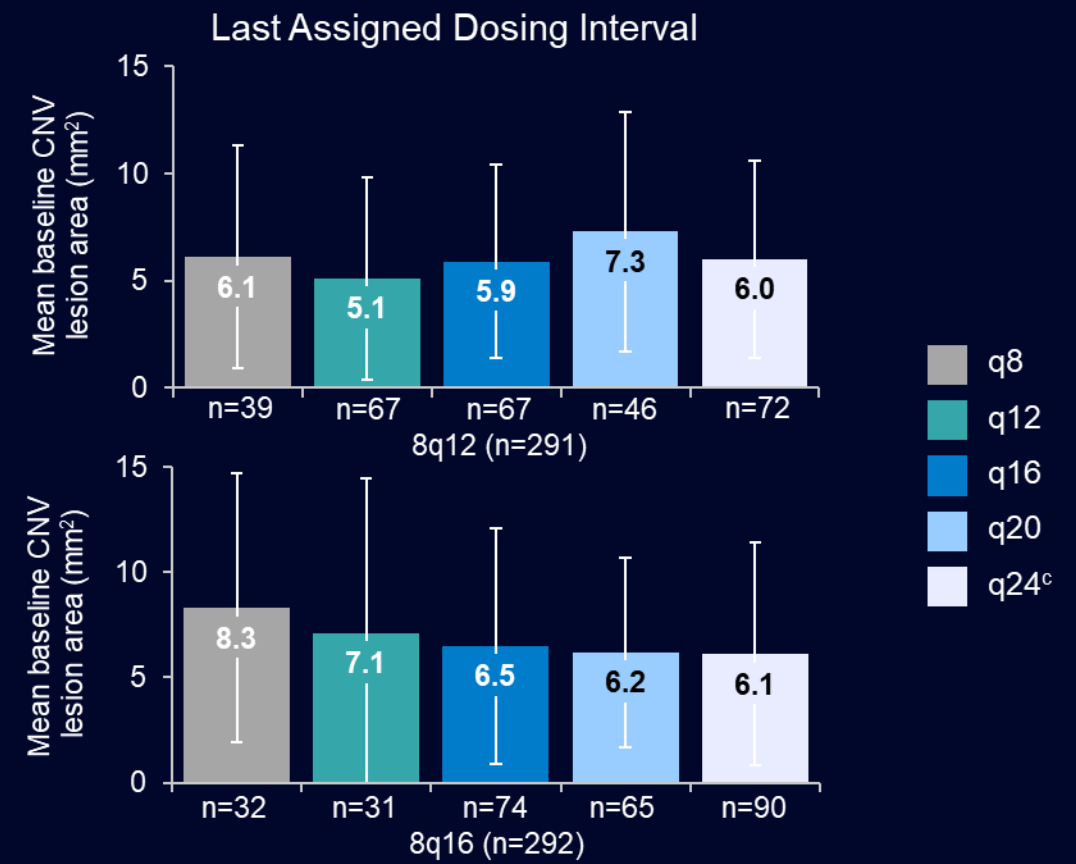
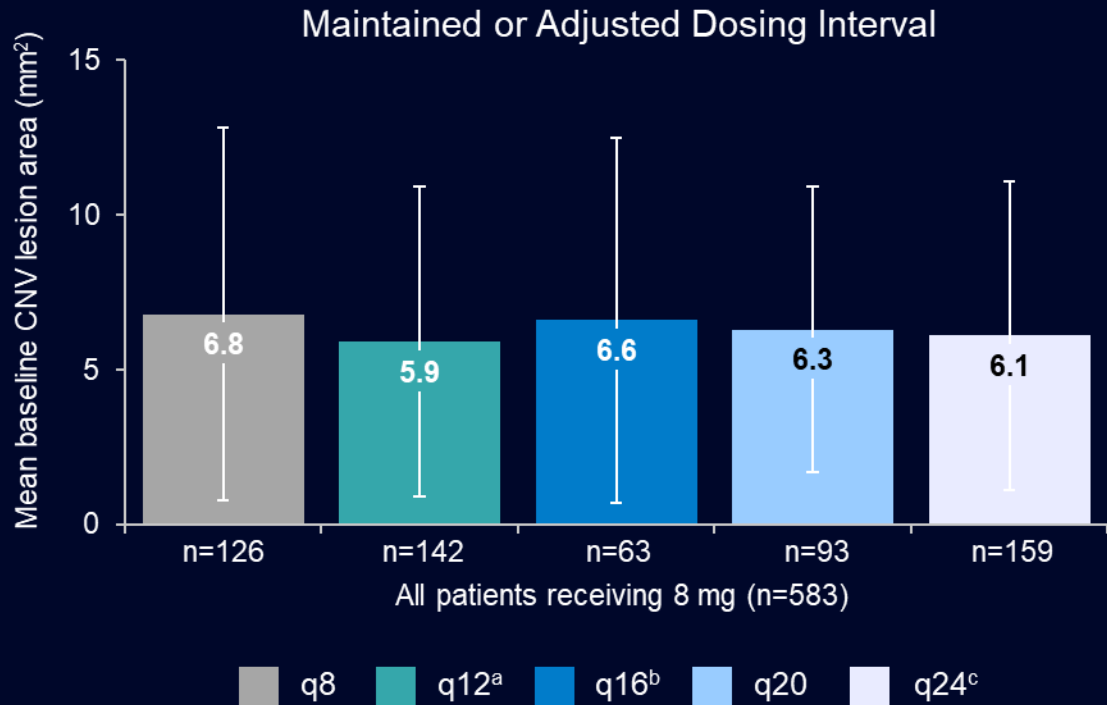


For patients receiving aflibercept 8 mg, **minor numerical differences in baseline CRT were observed across groups of patients** defined by maintained or adjusted dosing interval and according to the last assigned dosing interval at Week 96

Data shown for patients who completed 96 weeks of treatment. Error bars show SD.

^aIncludes patients randomly assigned to 8q12 whose dosing intervals were extended to q16, but not further and includes patients randomly assigned to 8q16 whose dosing intervals were shortened to q12, but not further. ^bIncludes patients randomly assigned to 8q16, whose dosing intervals were not shortened or extended. ^cPatients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

Baseline CNV Lesion Area According to Maintained or Adjusted and Last Assigned Dosing Interval Through Week 96



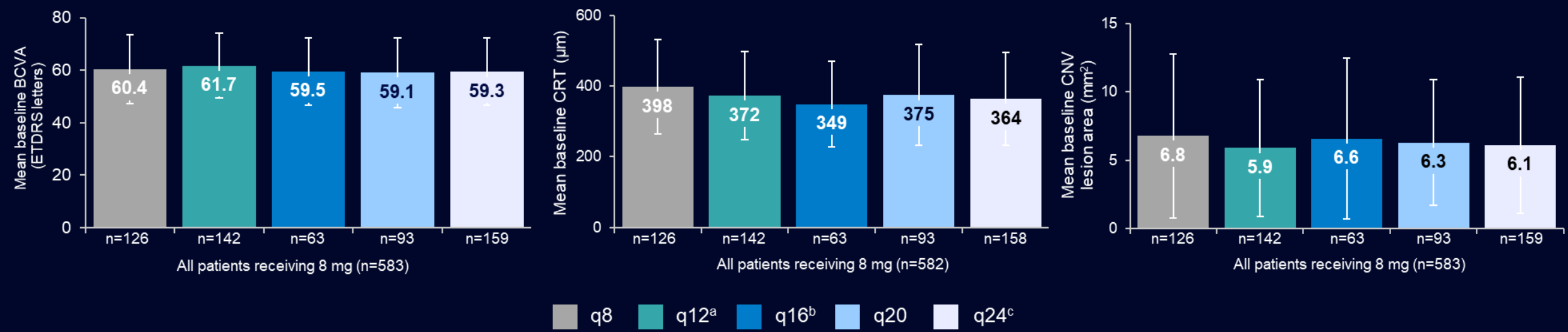
For patients receiving aflibercept 8 mg, **baseline CNV lesion area was similar across groups of patients** as defined by maintained or adjusted dosing interval and according to the last assigned dosing interval at Week 96

Data shown for patients who completed 96 weeks of treatment. Error bars show SD.
^aIncludes patients randomly assigned to 8q12 whose dosing intervals were extended to q16, but not further and includes patients randomly assigned to 8q16 whose dosing intervals were shortened to q12, but not further. ^bIncludes patients randomly assigned to 8q16, whose dosing intervals were not shortened or extended. ^cPatients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

Conclusions

- At Week 96, **71%** of patients receiving aflibercept 8 mg **were assigned \geq q16 dosing intervals** and 28% were assigned q24 dosing intervals
- This post hoc analysis of PULSAR showed **minor numerical differences in baseline BCVA, CRT, and CNV lesion area** across groups of patients defined by dosing interval throughout the study, suggesting that **all patients with nAMD have the potential to achieve extended dosing intervals** with aflibercept 8 mg **regardless of these baseline disease features**

Patients with Maintained, Extended, or Shortened Dosing Intervals by Baseline Characteristics at Week 96



Error bars denote SD.
^aIncludes patients randomly assigned to 8q12 whose dosing intervals were extended to q16, but not further and includes patients randomly assigned to 8q16 whose dosing intervals were shortened to q12, but not further. ^bIncludes patients randomly assigned to 8q16, whose dosing intervals were not shortened or extended. ^cPatients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

References

1. Lanzetta P, et al. *Lancet*. 2024;403:1141–1152.