Key Baseline Disease Characteristics in Neovascular Age-related Macular Degeneration Were Not Predictive of Dosing Interval Extension of Aflibercept 8 mg: A Post Hoc 96-week PULSAR Analysis

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Disclosures

- **Javier Zarranz-Ventura**: Speaker: Alcon, Alimera Sciences, Allergan, AbbVie, Bausch & Lomb, Bayer, Brill Pharma, DORC, Esteve, Novartis, Roche, Topcon Healthcare, and Zeiss; Research: AbbVie, Allergan Inc., Bayer, Novartis, Roche; Scientific advisor: AbbVie, Allergan Inc., Novartis, and Roche
- **JGG**: Consultant/speaker: AbbVie, Bayer, Novartis, and Roche; Research: Bayer, Novartis, and Roche. **PL**: Consultant: Aerie Pharmaceuticals, Allergan, Apellis, Bausch & Lomb, Bayer, Biogen, Boehringer Ingelheim, Eyepoint Pharmaceuticals, Genentech, I-Care, Novartis, Ocular Therapeutix, Outlook Therapeutics, and Roche. **VC**: Grants: Bayer, Novartis, and Roche; Advisory board member: Alcon, Appelis, Bayer, Boehringer Ingelheim, and Roche. **SL**, **TM**, and **XZ**: Employees of Bayer
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- This study includes research conducted on human patients. Institutional Review Board approval was obtained prior to study initiation
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PULSAR: Multicenter, Randomized, Double-masked Study

pulsar nAMD

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

[a]DRM: 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

[b]DRM: 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

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	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

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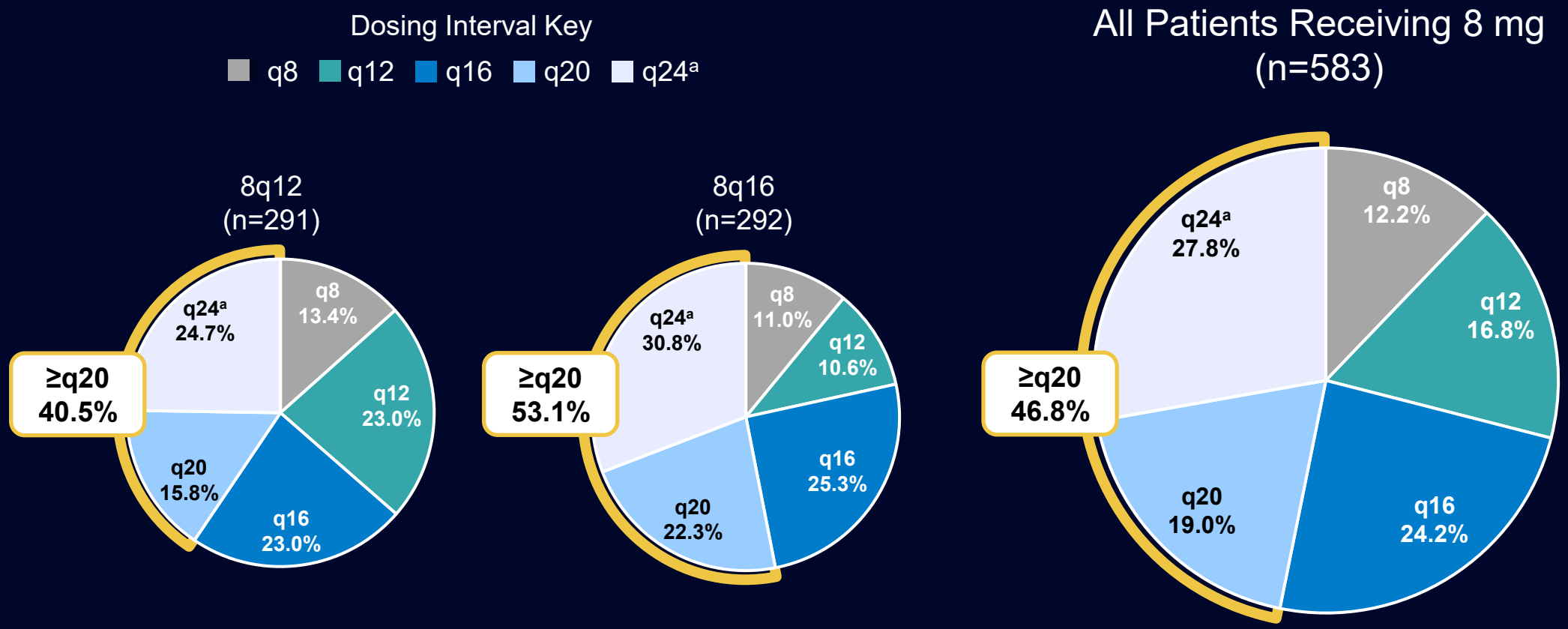
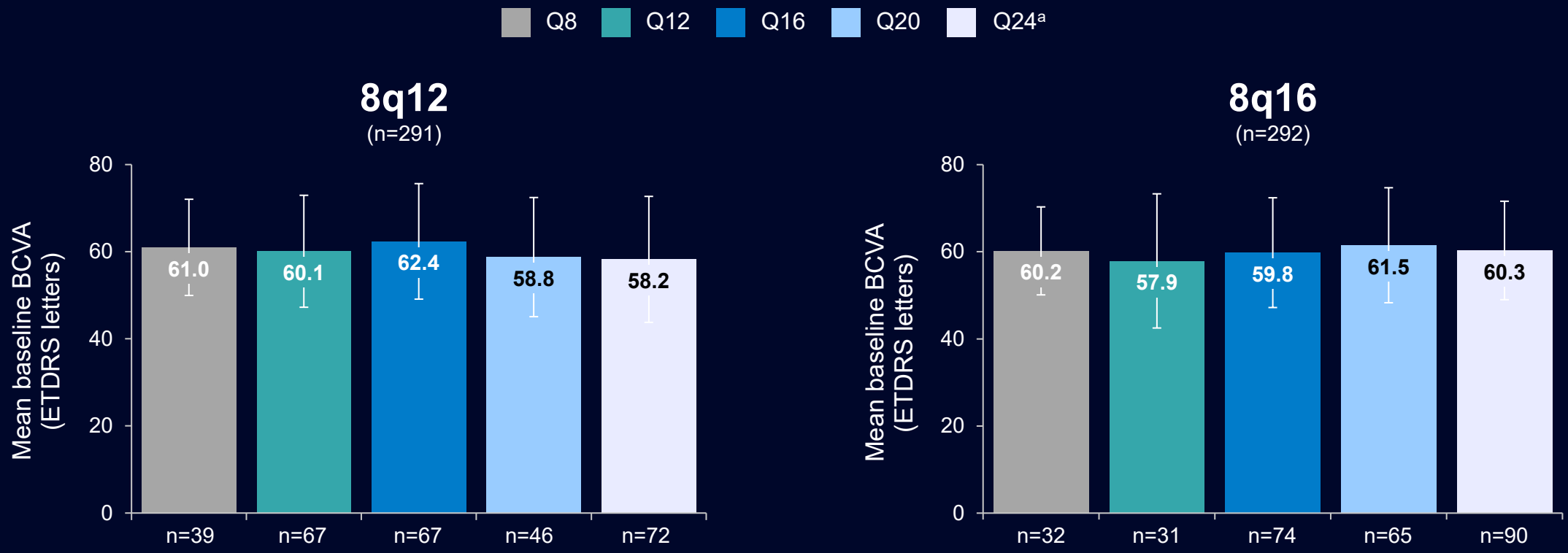


Purpose of this post hoc analysis was to evaluate baseline characteristics in patients treated with aflibercept 8 mg in groups defined according to the last assigned dosing interval

Data shown for patients who completed 96 weeks of treatment.
[a]Patients 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.

Baseline BCVA According to Last Assigned Dosing Interval Through Week 96

pulsar nAMD

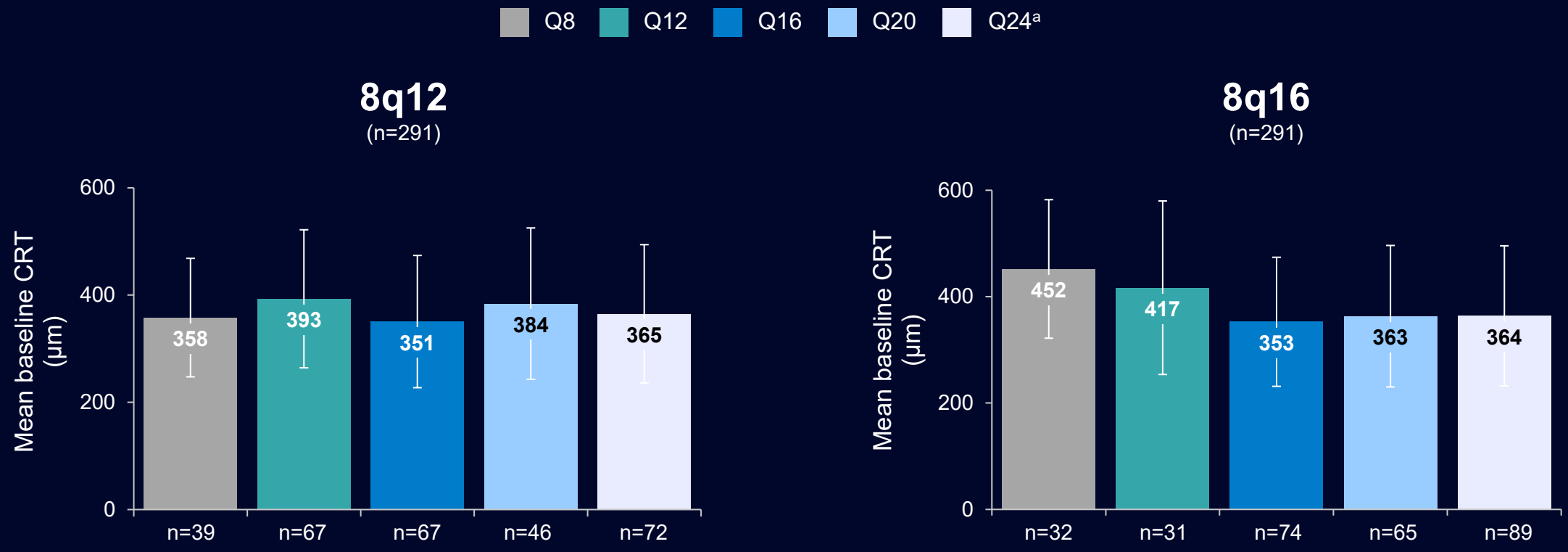


For patients receiving aflibercept 8 mg, **baseline BCVA was similar across groups of patients** defined according to the last assigned dosing interval at Week 96

Data shown for patients who completed 96 weeks of treatment. Error bars show SD.
[a]Patients 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 Last Assigned Dosing Interval Through Week 96

pulsar nAMD

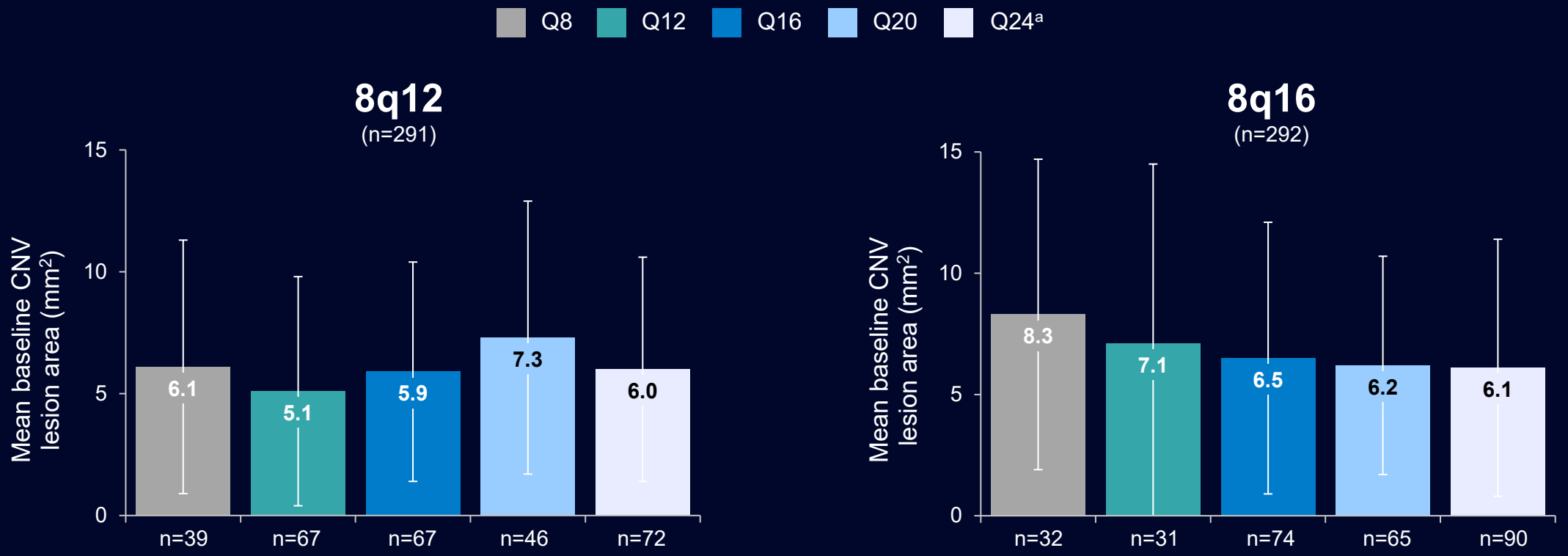


For patients receiving aflibercept 8 mg, **minor numerical differences in baseline CRT were observed across groups of patients** defined according to the last assigned dosing interval at Week 96

Data shown for patients who completed 96 weeks of treatment. Error bars show SD.
[a]Patients 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 Last Assigned Dosing Interval Through Week 96

pulsar nAMD



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

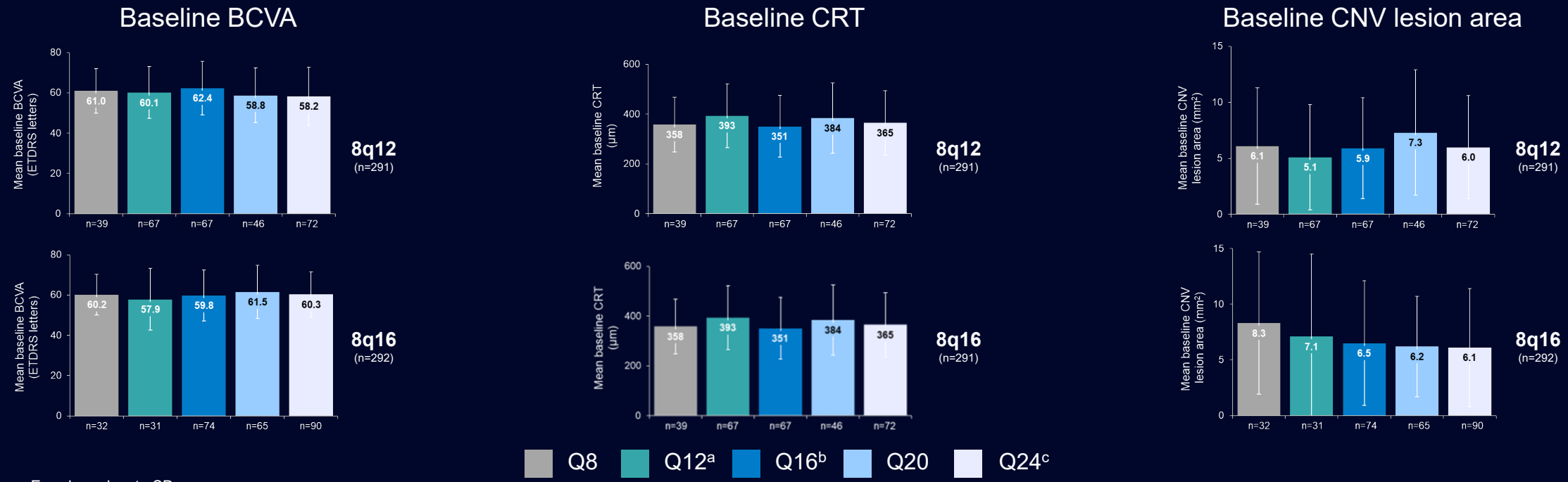
Data shown for patients who completed 96 weeks of treatment. Error bars show SD.
[a]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

Conclusions

pulsar nAMD

- At Week 96, **71%** of patients receiving aflibercept 8 mg **were assigned ≥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 according to the last assigned dosing interval at Week 96, 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 according to last assigned dosing interval through Week 96



Error bars denote SD.

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