Key baseline disease characteristics in nAMD are not linked to treatment interval extension of aflibercept 8 mg: A post-hoc 96-week PULSAR analysis

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Presented at the Association for Research in Vision and Ophthalmology 2024 Annual Meeting, May 5–9, 2024, Seattle, WA, USA

PULSAR: Multicenter, randomized, double-masked study

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Patients with treatment-naïve nAMD, randomized at baseline

2q8	8q12	8q16
Aflibercept 2 mg every 8 weeks after 3 initial monthly injections n=336	Aflibercept 8 mg every 12 weeks after 3 initial monthly injections n=335	Aflibercept 8 mg every 16 weeks after 3 initial monthly injections n=338

	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 central 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 retinal thickness; **DRM**, dose regimen modification; **nAMD**, neovascular age-related macular degeneration; **OCT**, optical coherence tomography; **W**, week.

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)
Total 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.
ETDRS, Early Treatment of Diabetic Retinopathy Study; **SD**, standard deviation.

Last assigned treatment intervals at Week 96 and objectives of this analysis

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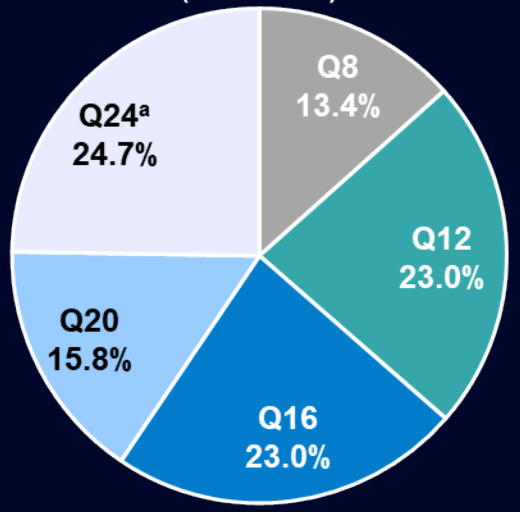
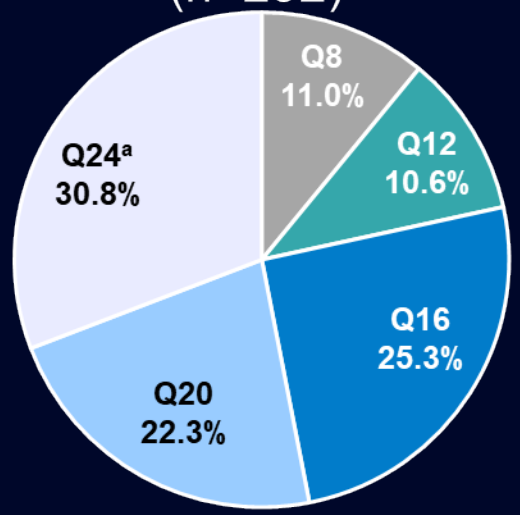
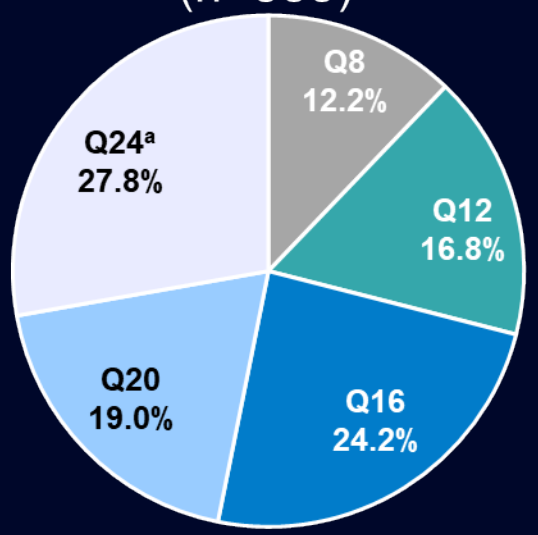
8q12 (n=291)



8q16 (n=292)



All patients receiving 8 mg (n=583)



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

1. According to whether treatment intervals were shortened, maintained, or extended
2. According to last assigned treatment 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.

q20, every 20 weeks.

Understanding treatment interval groupings through Week 96

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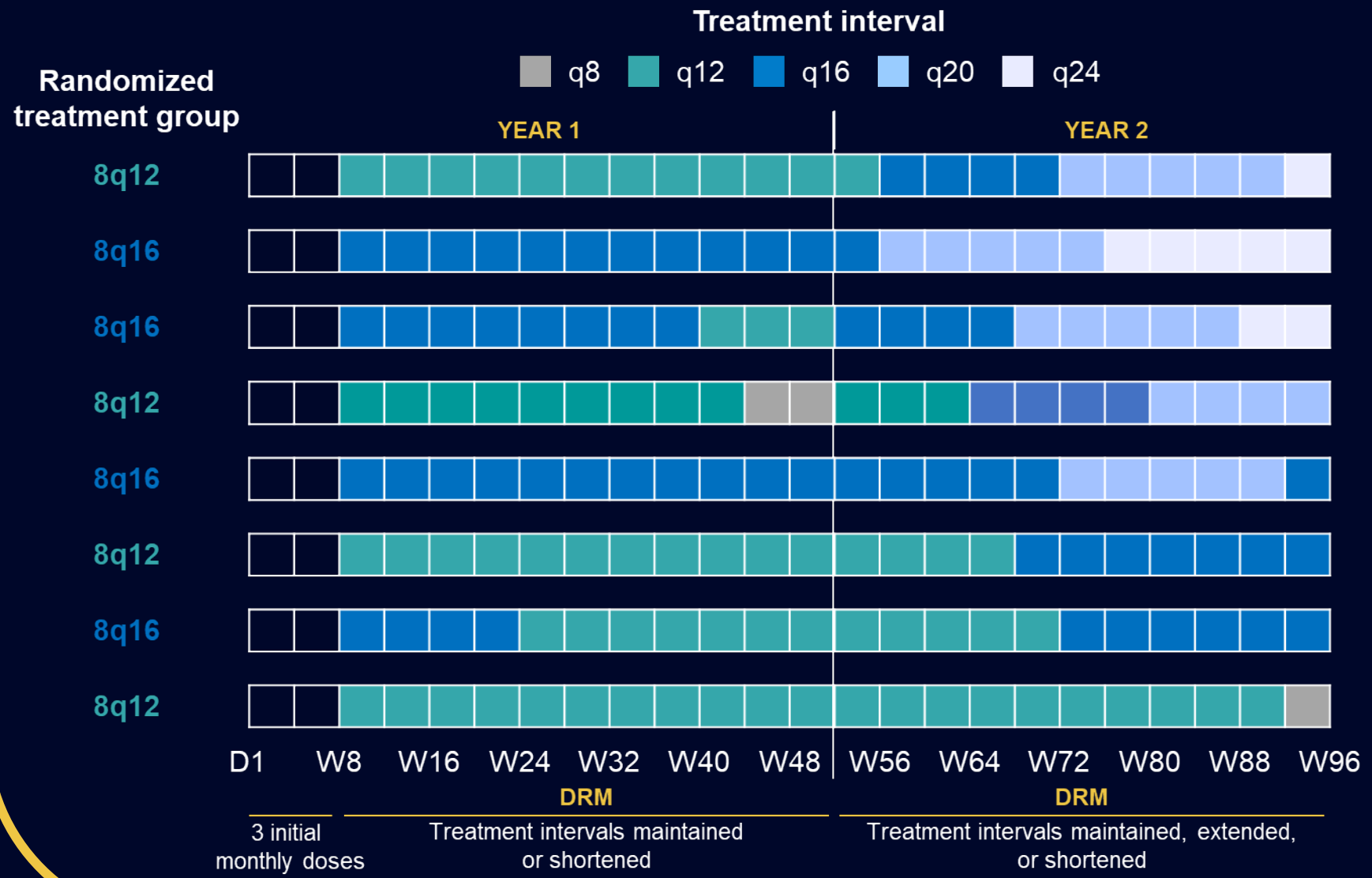
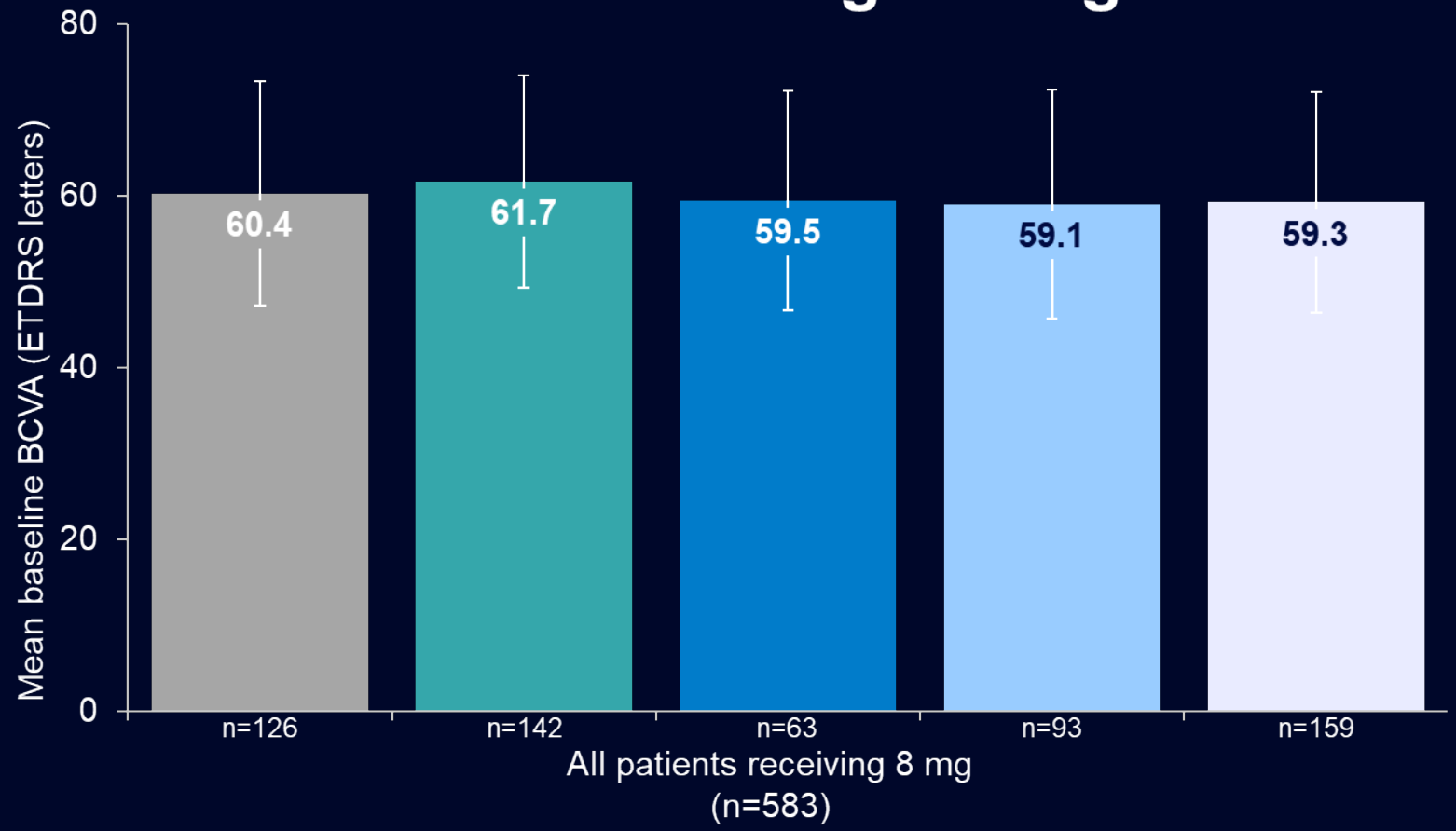


Treatment interval grouping	
Treatment interval through Week 96	Last assigned treatment interval
q24	q24
q24	q24
q12	q24
q8	q20
q16	q16
q12	q16
q12	q16
q8	q8

D, day.

Baseline BCVA according to dosing through Week 96

nAMD



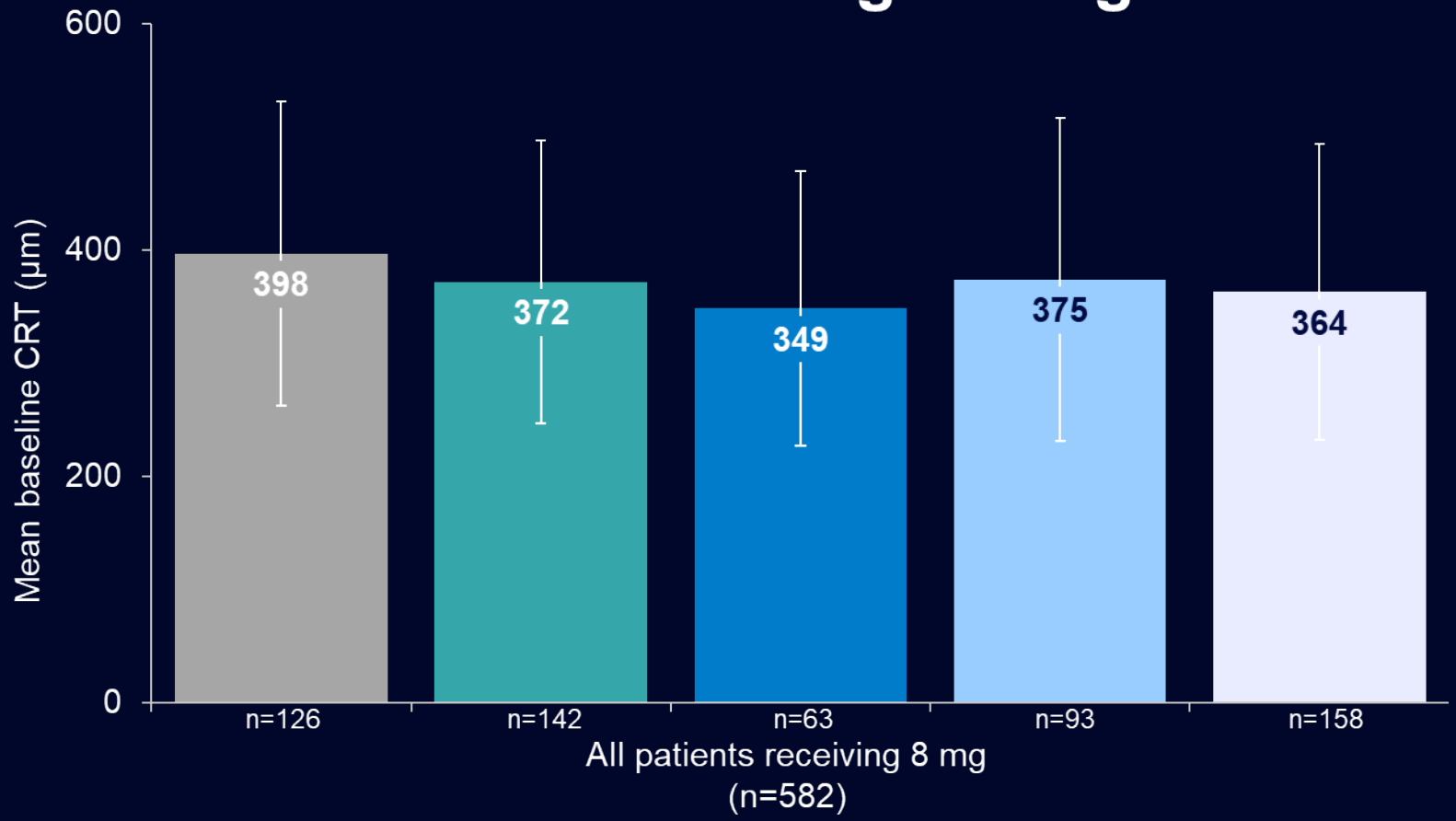
- Patients whose treatment intervals were **shortened to q8** at any point
- Patients whose treatment intervals were **maintained at q12** throughout the study[a]
- Patients whose treatment intervals were **maintained at q16** throughout the study[b]
- Patients whose treatment intervals were **maintained** per randomized schedule and then **extended to q20**, without interval shortening
- Patients whose treatment intervals were **maintained** per randomized schedule and then **extended to q24**[c], without interval shortening

For patients receiving aflibercept 8 mg, **baseline BCVA was similar across groups of patients** as defined by dosing interval throughout the study

Data shown for patients who completed 96 weeks of treatment. Error bars show SD.
[a]Includes patients randomly assigned to 8q12 whose intervals were extended to q16, but not further and includes patients randomly assigned to 8q16 whose intervals were shortened to q12, but not further. [b]Includes patients randomly assigned to 8q16, whose dosing intervals were not shortened or extended. [c]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 dosing through Week 96

nAMD



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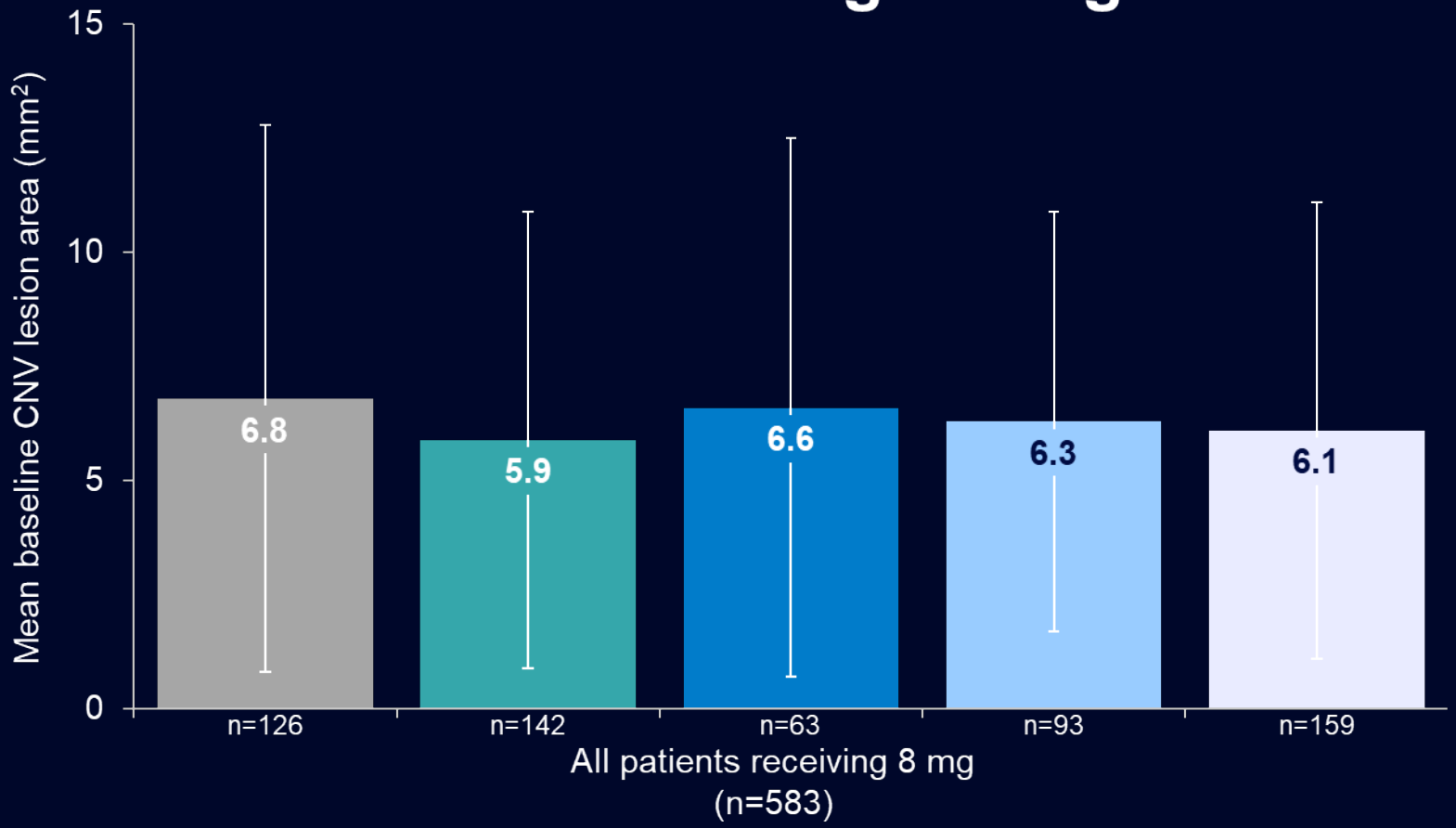
- Patients whose treatment intervals were **maintained** per randomized schedule and then **extended to q24**[c], without interval shortening

For patients receiving aflibercept 8 mg, **minor numerical differences in baseline CRT were observed across groups of patients** defined by dosing interval throughout the study

Data shown for patients who completed 96 weeks of treatment. Error bars show SD.
[a]Includes patients randomly assigned to 8q12 whose intervals were extended to q16, but not further and includes patients randomly assigned to 8q16 whose intervals were shortened to q12, but not further. [b]Includes patients randomly assigned to 8q16, whose dosing intervals were not shortened or extended. [c]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 size according to dosing through Week 96

nAMD



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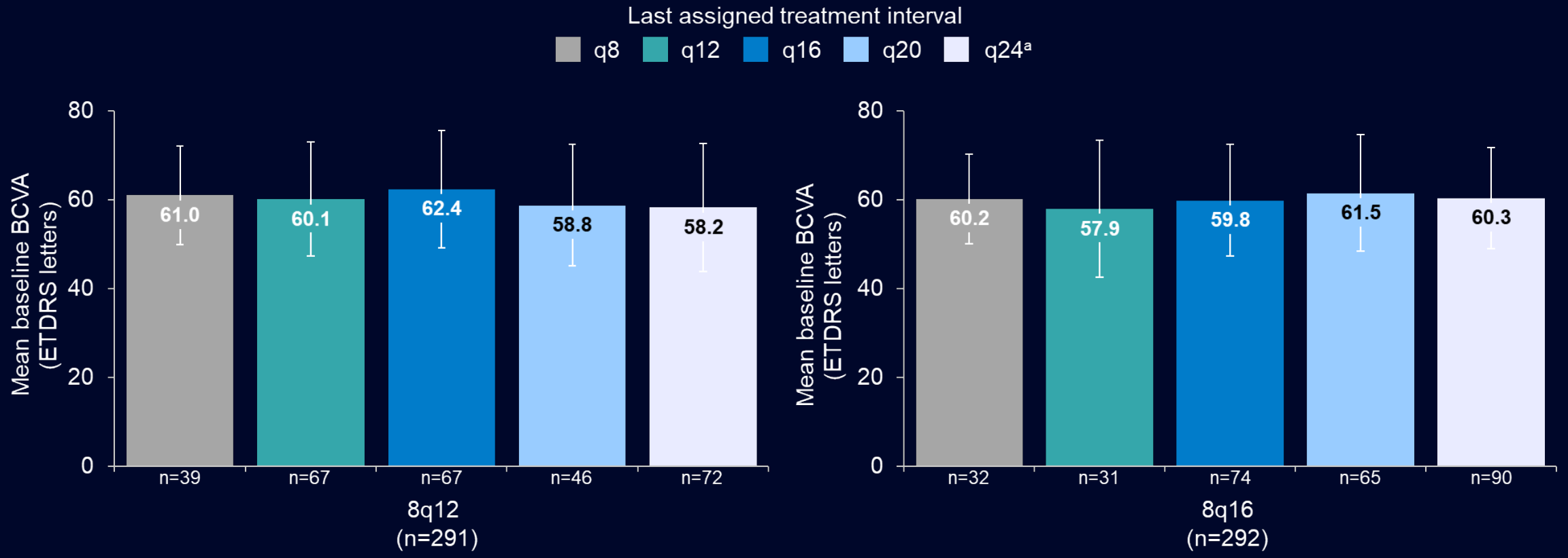
For patients receiving aflibercept 8 mg, **baseline CNV lesion area was similar across groups of patients** as defined by dosing interval throughout the study

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

[a]Includes patients randomly assigned to 8q12 whose intervals were extended to q16, but not further and includes patients randomly assigned to 8q16 whose intervals were shortened to q12, but not further. [b]Includes patients randomly assigned to 8q16, whose dosing intervals were not shortened or extended. [c]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

CNV, choroidal neovascularization.

Baseline BCVA according to last assigned treatment intervals at Week 96



For patients receiving aflibercept 8 mg, **baseline BCVA was similar across all groups** defined according to the last assigned treatment intervals 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 treatment intervals at Week 96

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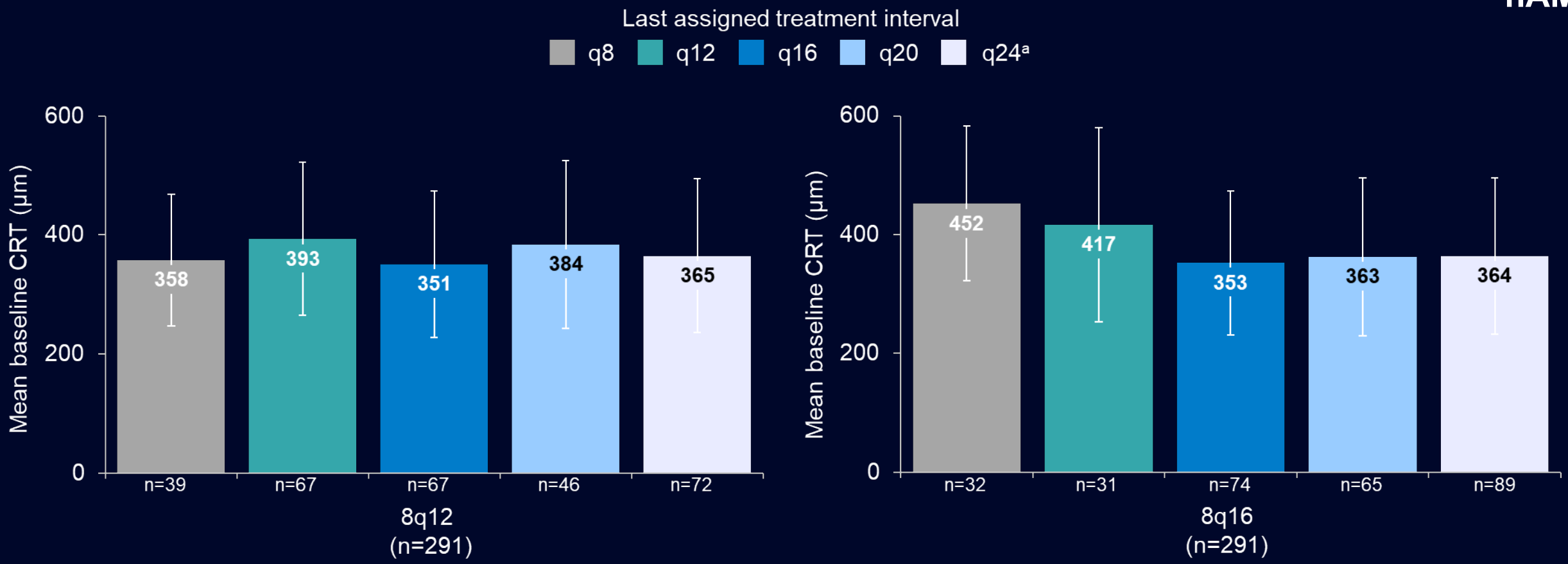
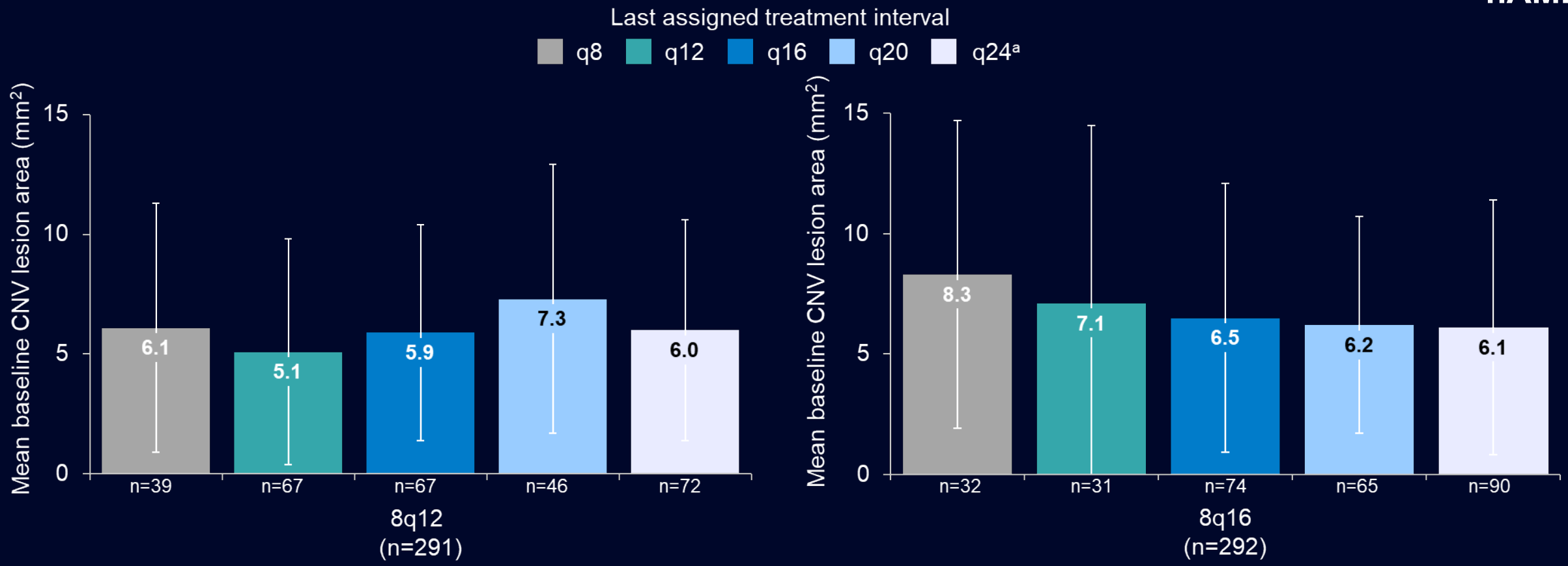


For patients receiving aflibercept 8 mg, **minor numerical differences in baseline CRT were observed across groups of patients** defined according to the last assigned treatment intervals at Week 96

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 size according to last assigned treatment intervals at Week 96

nAMD



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

Data shown for patients who completed 96 weeks of treatment. Data are mean. 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

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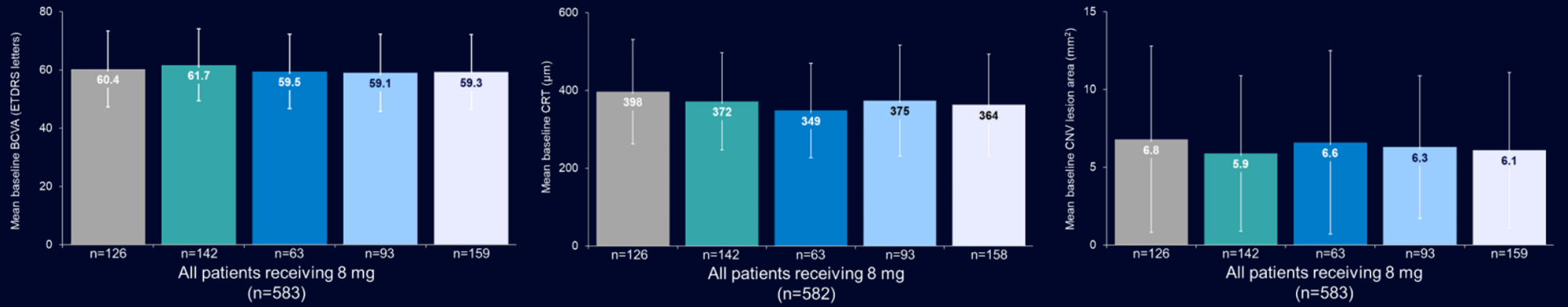
- At Week 96, **71%** of patients receiving aflibercept 8 mg **had ≥q16 treatment intervals** and >27% had q24 treatment intervals
- This post-hoc analysis of PULSAR showed **minor numerical differences in baseline BCVA, CRT, and CNV size** across groups of patients defined by dosing interval throughout the study, suggesting that all nAMD patients have the potential to achieve extended treatment intervals with aflibercept 8 mg regardless of these baseline disease features

Patients with maintained, extended, or shortened dosing intervals, by baseline characteristics



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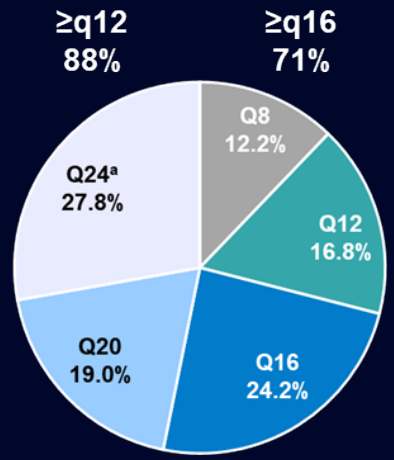
Last assigned treatment interval



All patients receiving 8 mg
(n=583)

Values may not add up to 100% due to rounding. Error bars denote SD.
[a]Includes patients randomly assigned to 8q12 whose intervals were extended to q16, but not further and includes patients randomly assigned to 8q16 whose intervals were shortened to q12, but not further. [b]Includes patients randomly assigned to 8q16, whose dosing intervals were not shortened or extended. [c]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

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Thank you!

- The PULSAR study (NCT04423718) was sponsored by Bayer AG (Leverkusen, Germany) and co-funded by Regeneron Pharmaceuticals, Inc. (Tarrytown, NY, USA). The sponsor participated in the design and conduct of the study, analysis of the data, and preparation of this presentation
- 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)