Key Baseline Disease Characteristics in nAMD Are Not Linked to Treatment Interval Extension of Aflibercept 8 mg: A Post hoc 96-week PULSAR Analysis

Javier Zarranz-Ventura,[1] Justus G. Garweg,[2] Paolo Lanzetta,[3] Varun Chaudhary,[4] Sergio Leal,[5] Tobias Machewitz,[6] Xin Zhang,[5] on behalf of the PULSAR study investigators

[1]Hospital Clínic de Barcelona, University of Barcelona, Barcelona, Spain; [2]Swiss Eye Institute and Berner Augenklinik, Bern, Switzerland; [3]Department of Medicine – Ophthalmology, University of Udine, and Istituto Europeo di Microchirurgia Oculare – IEMO, Udine-Milan, Italy; [4]Hamilton Regional Eye Institute, St. Joseph's Healthcare Hamilton, McMaster University, Hamilton, ON, Canada; [5]Bayer Consumer Care AG, Basel, Switzerland; [6]Bayer AG, Berlin, Germany

Presented at the 24th European Society of Retina Specialists (EURETINA), Barcelona, Spain, September 19–22, 2024

Disclosures

- **Javier Zarranz-Ventura**: Speaker: Alcon, Alimera Sciences, Allergan, AbbVie, Bausch & Lomb, Bayer, Brill Pharma, DORC, Esteve, Novartis, Roche, Topcon Healthcare, Zeiss; Research: AbbVie, Allergan Inc, Bayer, Novartis, Roche; Scientific advisor: AbbVie, Allergan Inc, Bayer, Novartis, and Roche
- **JGG**: Consultant/speaker: AbbVie, Bayer, Novartis, and Roche; Research: Bayer, Novartis, and Roche. **PL**: Consultant: Aerie, Allergan, Apellis, Bausch & Lomb, Bayer, Biogen, Boehringer Ingelheim, Genentech, I-Care, Novartis, Outlook Therapeutics, and Roche. **VC**: Research: Bayer Healthcare, Novartis Pharma AG, and Roche; Scientific advisor: Alcon Laboratories, Apellis, Bayer Healthcare, Boehringer Ingelheim, Novartis Pharma AG, and Roche. **SL**, **TM**, and **XZ**: Employees of Bayer
- 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
- This study includes research conducted on human patients. Institutional Review Board approval was obtained prior to study initiation
- Medical writing support, under the direction of the authors, was provided by ApotheCom and funded by Bayer Consumer Care AG (Basel, Switzerland), in accordance with Good Publication Practice (GPP) guidance (*Ann Intern Med* 2022;175:1298–1304)
- Data originally presented at ARVO 2024 Annual Meeting; May 5–9, 2024; Seattle, WA, USA

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.

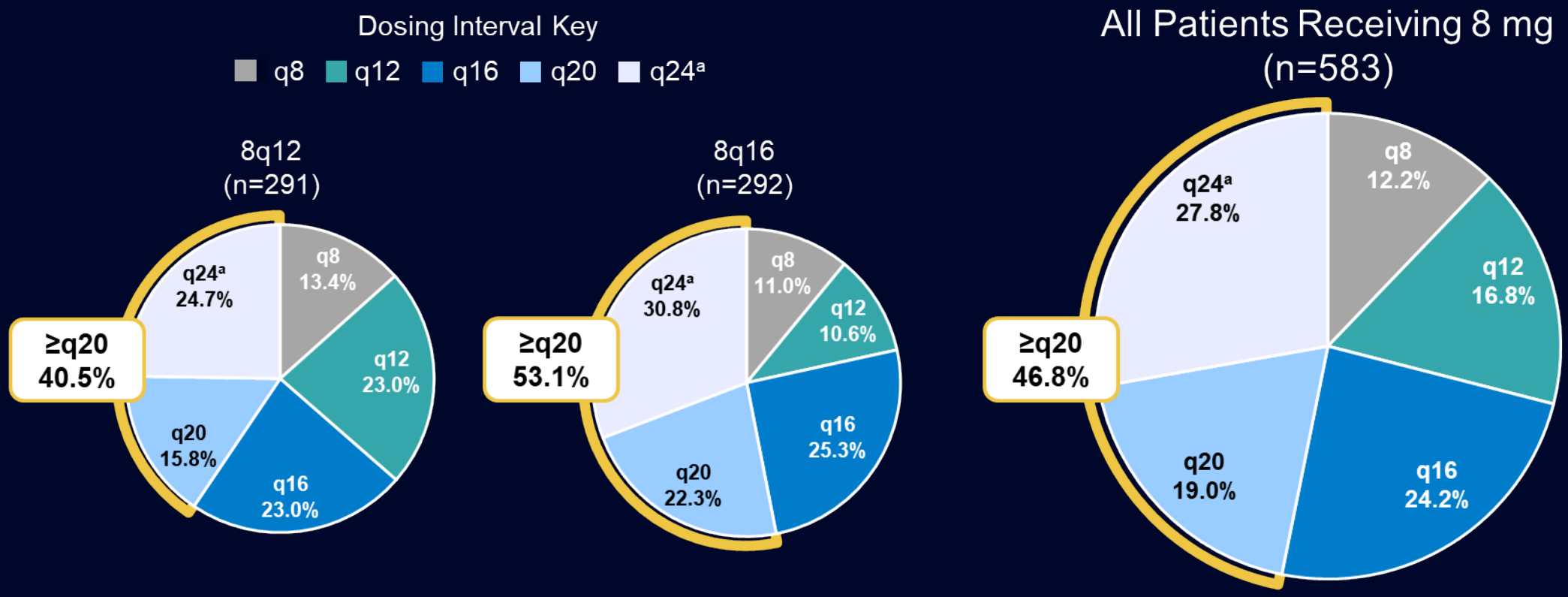
Baseline Demographics and Study Eye Characteristics

pulsar nAMD

	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



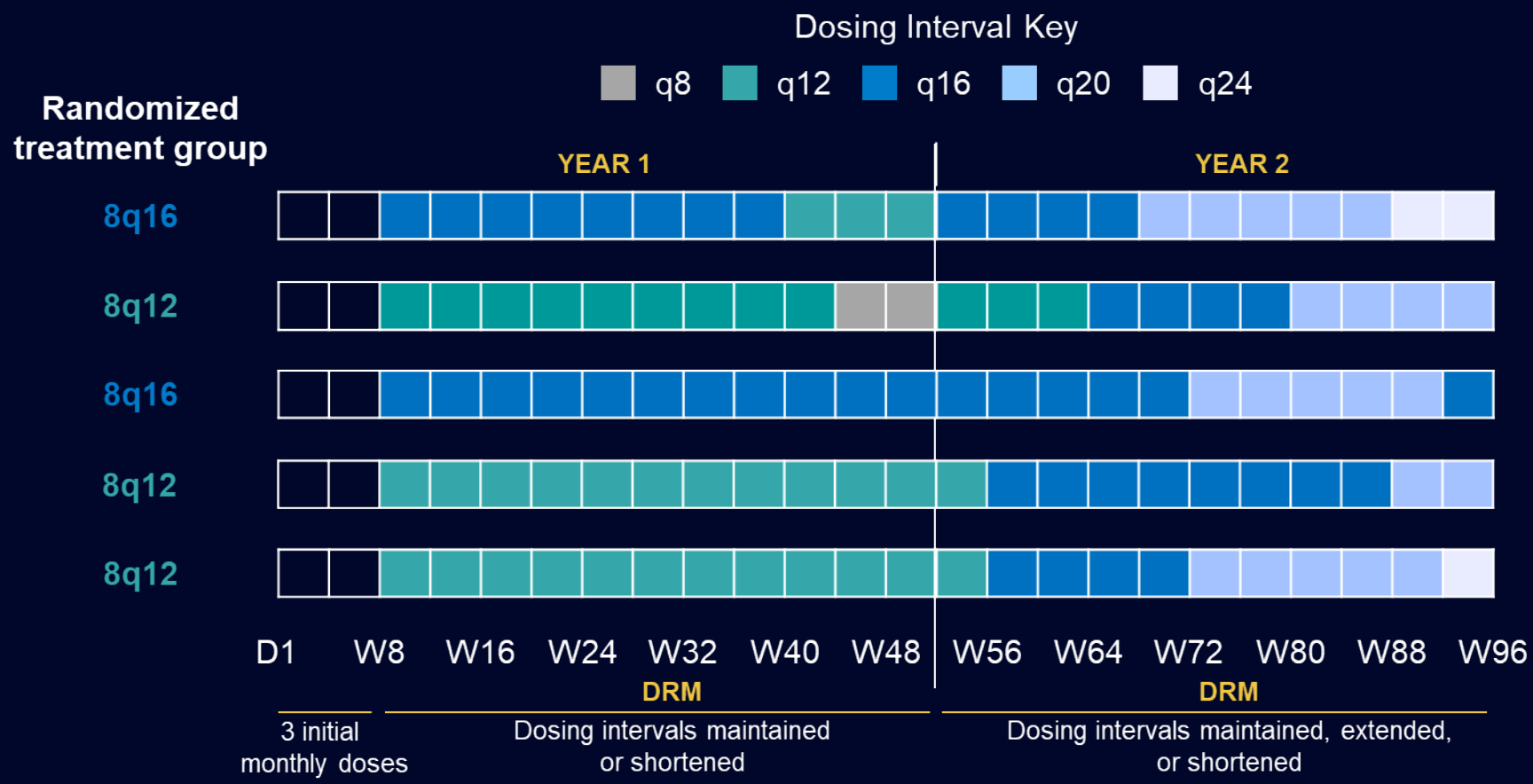
Purpose of this post hoc analysis was to **evaluate baseline characteristics in patients treated with aflibercept 8 mg** in groups defined by dosing intervals in 2 different ways:

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.
[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.

Understanding Dosing Interval Groupings Through Week 96

pulsar nAMD



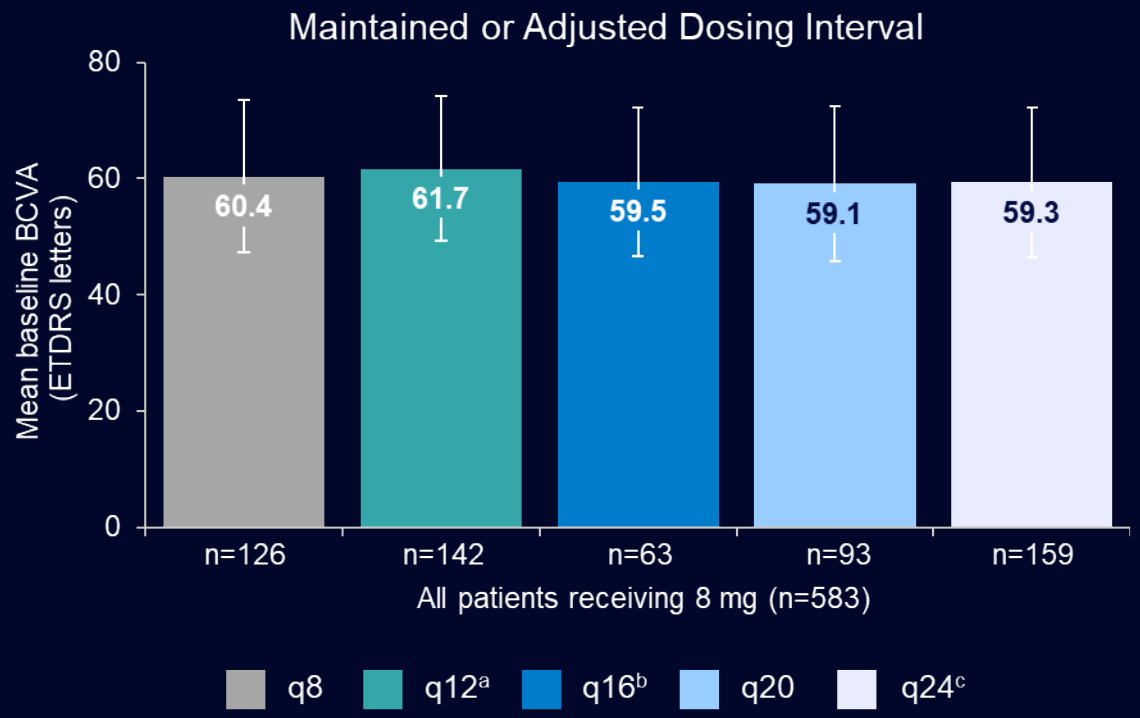
Dosing Interval Grouping

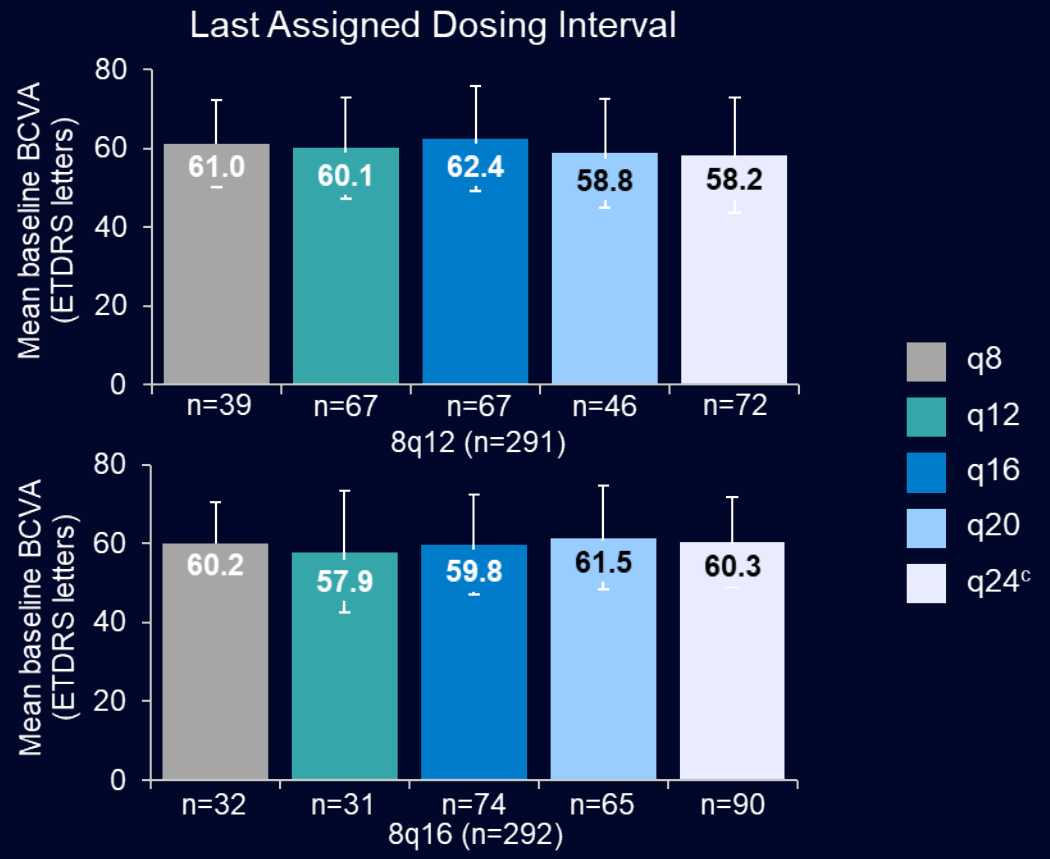
Maintained or adjusted dosing interval[a]		Last assigned dosing interval
q12	Shortened to q12 at any point	q24
q8	Shortened to q8 at any point	q20
q16	Maintained at q16	q16
q20	Extended to q20	q20
q24	Extended to q24[b]	q24

[a]Defined 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. [b]Patients 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

nAMD



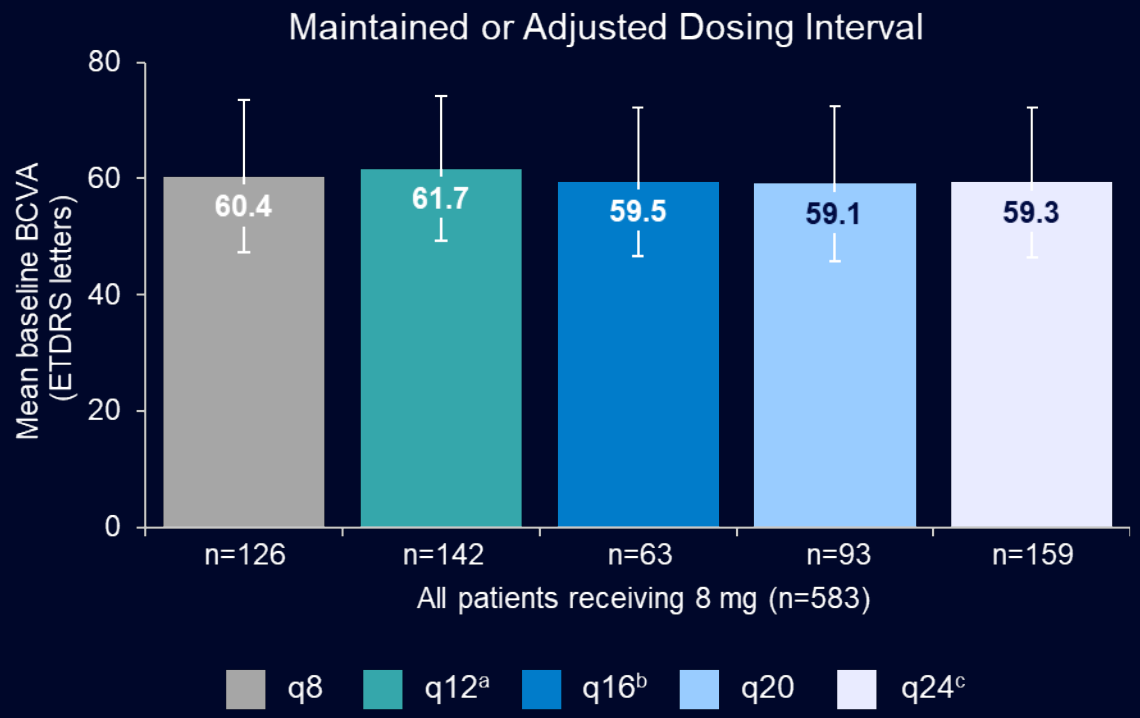


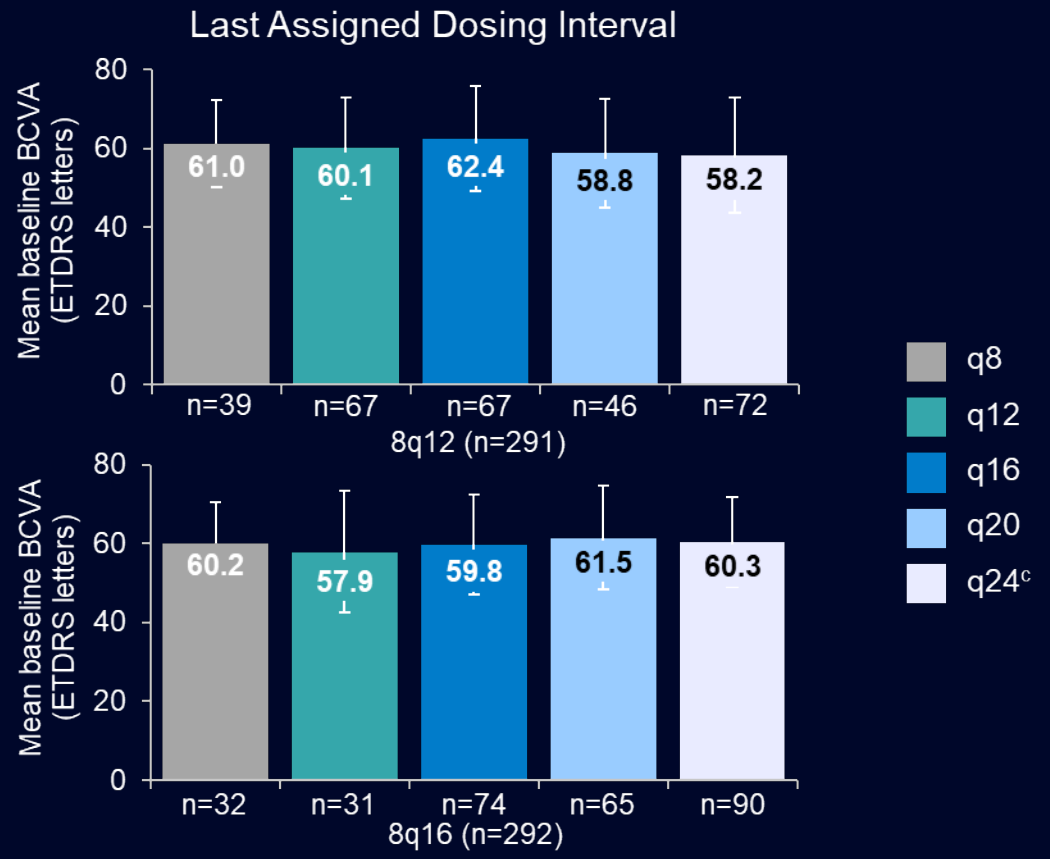
For patients receiving aflibercept 8 mg, **baseline BCVA was similar across groups of patients** as defined by maintained or adjusted dosing interval and according to the last assigned dosing interval at Week 96

Data shown for patients who completed 96 weeks of treatment. Error bars show SD.
[a]Includes 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. [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 BCVA According to Maintained or Adjusted and Last Assigned Dosing Interval Through Week 96

nAMD



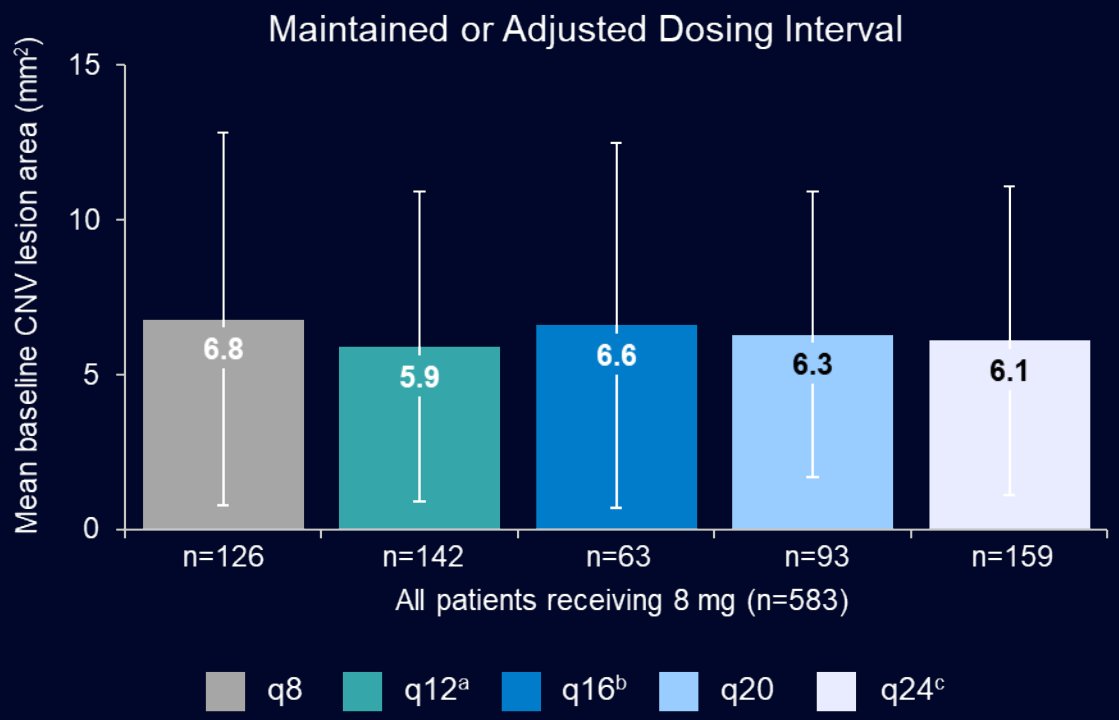


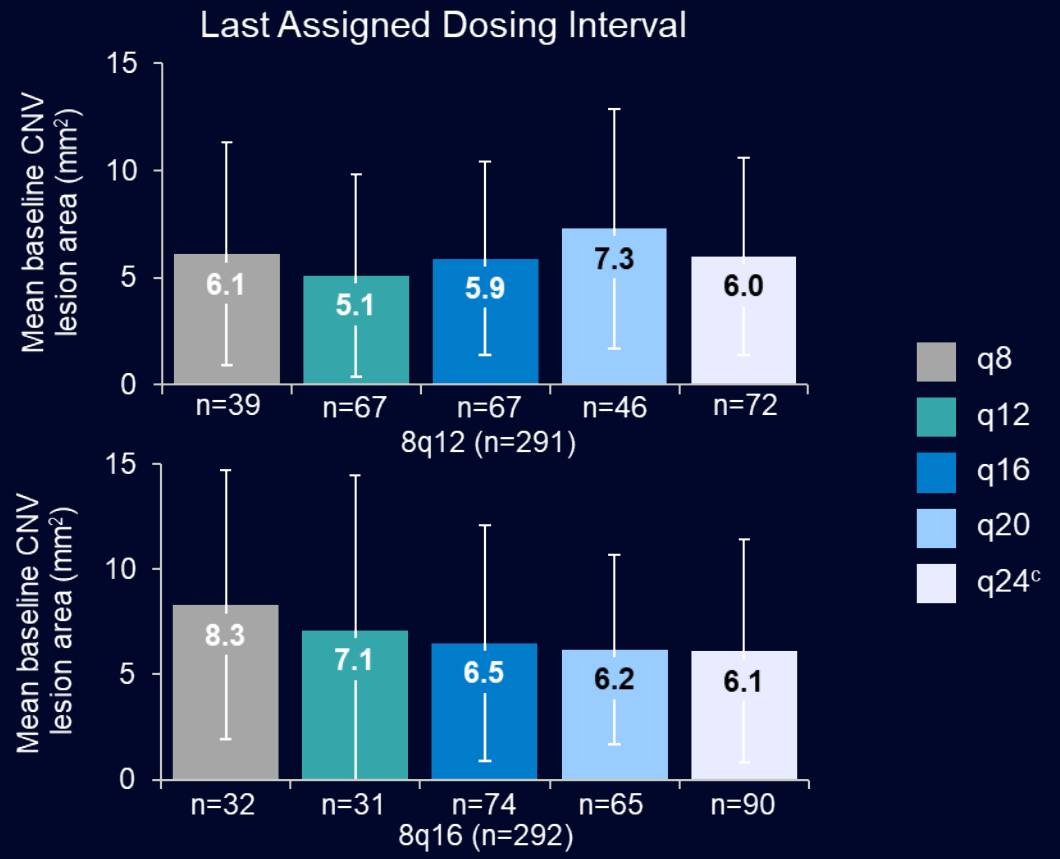
For patients receiving aflibercept 8 mg, **baseline BCVA was similar across groups of patients** as defined by maintained or adjusted dosing interval and according to the last assigned dosing interval at Week 96

Data shown for patients who completed 96 weeks of treatment. Error bars show SD.
[a]Includes 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. [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 Area According to Maintained or Adjusted and 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** as defined by maintained or adjusted dosing interval and according to the last assigned dosing interval at Week 96

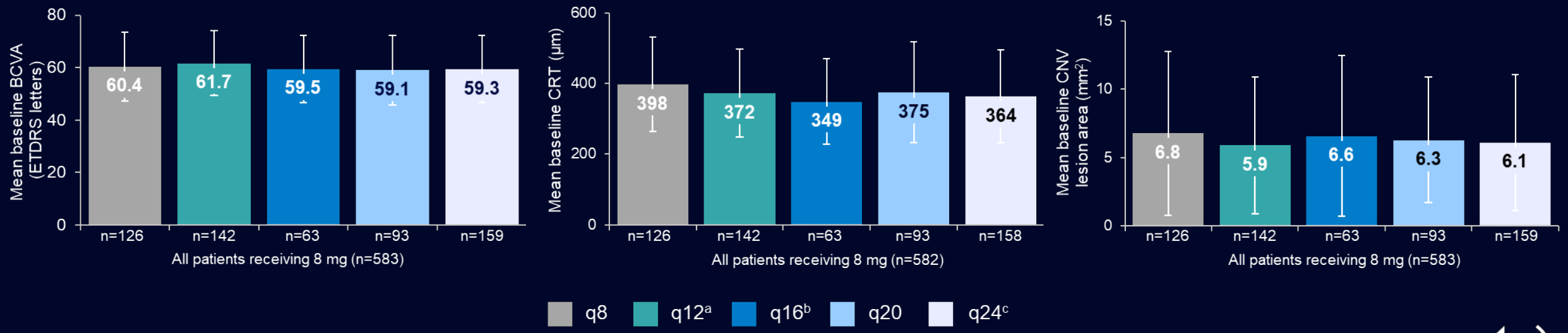
Data shown for patients who completed 96 weeks of treatment. Error bars show SD.
[a]Includes patients randomly assigned to 8q12 whose dosing intervals were extended to q16, but not further and includes patients randomly assigned to 8q16 whose dosing intervals were shortened to q12, but not further. [b]Includes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

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 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.

[a]Includes 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. [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.