PULSAR Extension: Clinical Improvements Sustained Over 156 Weeks With Aflibercept 8 mg in Patients With Neovascular Age-Related Macular Degeneration

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Disclosures

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PULSAR Extension Design

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PULSAR (BL–W96)
(Masked)

Patients with treatment-naïve nAMD

2q8 arm (n=336)
Aflibercept 2 mg every 8 weeks after 3 initial monthly injections

8q12 arm (n=335)
Aflibercept 8 mg every 12 weeks after 3 initial monthly injections

8q16 arm (n=338)
Aflibercept 8 mg every 16 weeks after 3 initial monthly injections

PULSAR Extension (W96–W156)
(Open-label and optional)[a]

2q8→8mg arm (n=208)
Patients originally assigned to 2q8 switched to aflibercept 8 mg every 12 weeks

8mg arm (n=417)
Patients originally assigned to 8q12 or 8q16 continued aflibercept 8 mg on last assigned dosing interval

Primary endpoint
Change from baseline in BCVA (non-inferiority)

N-BL[b]

Start of PULSAR Extension[c]

Dosing interval modifications through W152

End of PULSAR Extension

Week: 0, 48, 84, 88, 92, 96, 100, 104, 108, 120, 132, 144, 156

= mandatory visits

[a]To be eligible for PULSAR Extension, patients had to have ≥1 BCVA and CRT assessments between Week 84 and Week 92. Masked transition period (W96–108) was followed by open-label part (W108–W156).
[b]N-BL was an average of values from W84, 88, and 92. [c]Optional phase added while PULSAR was ongoing; therefore, not all patients were able to enroll due to time constraints.
2q8, aflibercept 2 mg every 8 weeks; **8q12,** aflibercept 8 mg every 12 weeks; **8q16**, aflibercept 8 mg every 16 weeks; **BCVA,** best-corrected visual acuity; **BL,** baseline; **CRT**, central subfield retinal thickness; **nAMD**, neovascular age-related macular degeneration; **N-BL**, new baseline; **W**, week.

Patient Disposition and Baseline Characteristics

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	PULSAR	PULSAR Extension		
	Total	2q8→8mg	8mg	Total
Patients entering PULSAR study (FAS), n	1009	–	–	–
Patients entering PULSAR Extension (eFAS), n (%)	–	208 (61.9)[a]	417 (62.0)[a]	625 (61.9)[a]
Completion rate at Week 96, %	85.9	–	–	–
Completion rate at Week 156, %	–	89.9[b]	90.4[b]	90.2[b]
Age (years)	74 (8.4)	73.9 (8.2)	74.0 (8.1)	74.0 (8.1)
Female, %	54.5	58.7	55.2	56.3
Race, %				
White	75.8	77.4	77.5	77.4
Black or African American	0.4	0.5	0.5	0.5
Asian	23.2	22.1	21.1	21.4
Other[c]	0.6	0	1.0	0.6
History of hypertension, %	64.3	63.0	65.0	64.3
BCVA (ETDRS letters)	59.6 (13.3)	59.6 (13.7)	60.6 (12.7)	60.3 (13.0)
CRT (μm)[d]	369 (130)	365 (139)	375 (132)	371 (134)
Total lesion area, mm^2	6.7 (5.4)	6.8 (5.0)	6.4 (5.2)	6.6 (5.1)
Lesion type, %				
Occult	58.2	57.7	57.1	57.5
Predominantly classic	20.7	23.1	22.4	18.8
Minimally classic	18.6	15.9	18.1	20.3

Data are mean±SD unless otherwise stated; data are for patients in the FAS (PULSAR) and eFAS (PULSAR Extension) at the main study baseline. [a]Proportions were calculated based on the number of patients who initially entered the main PULSAR study. [b]Completion rate for PULSAR Extension based on eFAS. [c]Other includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, multiple races, and unreported race. [d]Data as assessed by reading center. **eFAS**, PULSAR Extension FAS; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **FAS**, full analysis set, **SD**, standard deviation.

Mean BCVA Through Week 156[a]

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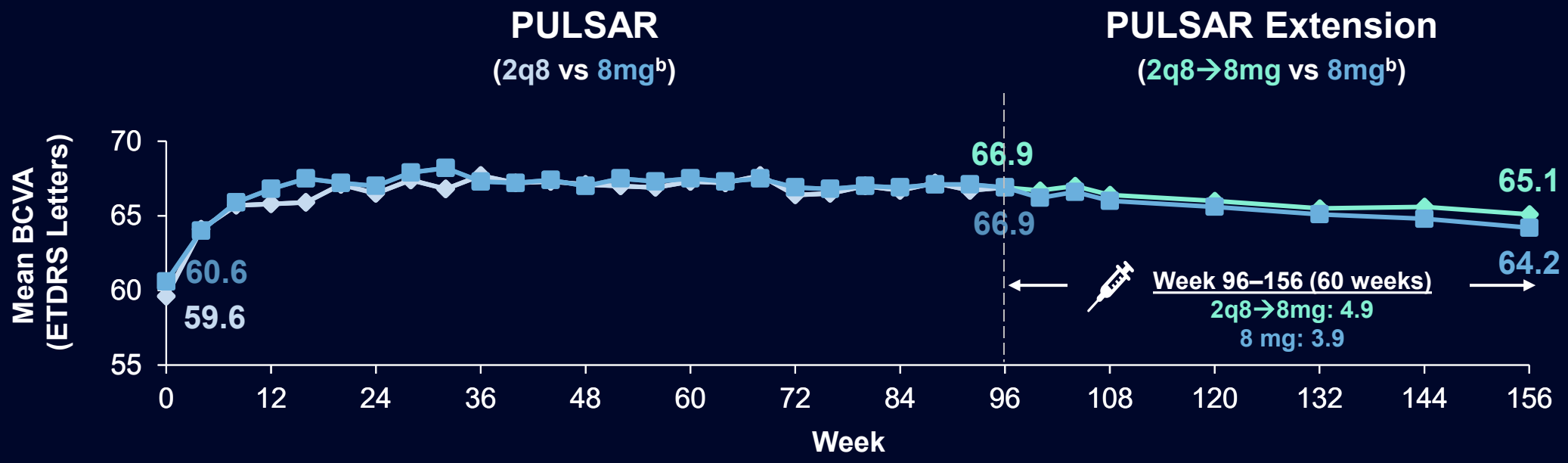

Mean number of active injections over 48-week periods:[c]

BL–Week 48
2 mg: 6.9
8q12: 6.1
8q16: 5.2

Week 48–96
2 mg: 5.9
8q12: 3.6
8q16: 3.1

Week 108–156
8 mg: 2.9
8 mg: 2.9

Note: At Week 156, the 2q8→8mg group (n=208) and 8mg group (n=417) reported LS mean (95% CI) changes from baseline (MMRM) in BCVA of +4.6 (2.6, 6.6) letters and +3.4 (1.9, 4.9) letters, respectively. MMRM was used to generate BCVA LS means for the eFAS with baseline BCVA as a covariate; treatment group (aflibercept 8q12, 8q16, 2q8), visit, and stratification variables (geographic region [Japan vs rest of the world] and baseline BCVA [<60 vs ≥60 letters]) as fixed factors; and terms for the interaction between visit and baseline BCVA and the interaction between visit and treatment. [a]eFAS (observed cases). [b]Patients who were randomly assigned to the 8q12 or 8q16 groups at the beginning of the PULSAR study and continued treatment with aflibercept 8 mg through the PULSAR Extension. [c]eSAF (156-week completers; 2q8→8mg, n=186; 8q12, n=185; 8q16, n=190; 8mg, n=375). **CI,** confidence interval; **eSAF**, safety analysis set in the PULSAR Extension; **LS**, least squares; **MMRM,** mixed model for repeated measures.

Mean CRT Through Week 156[a]

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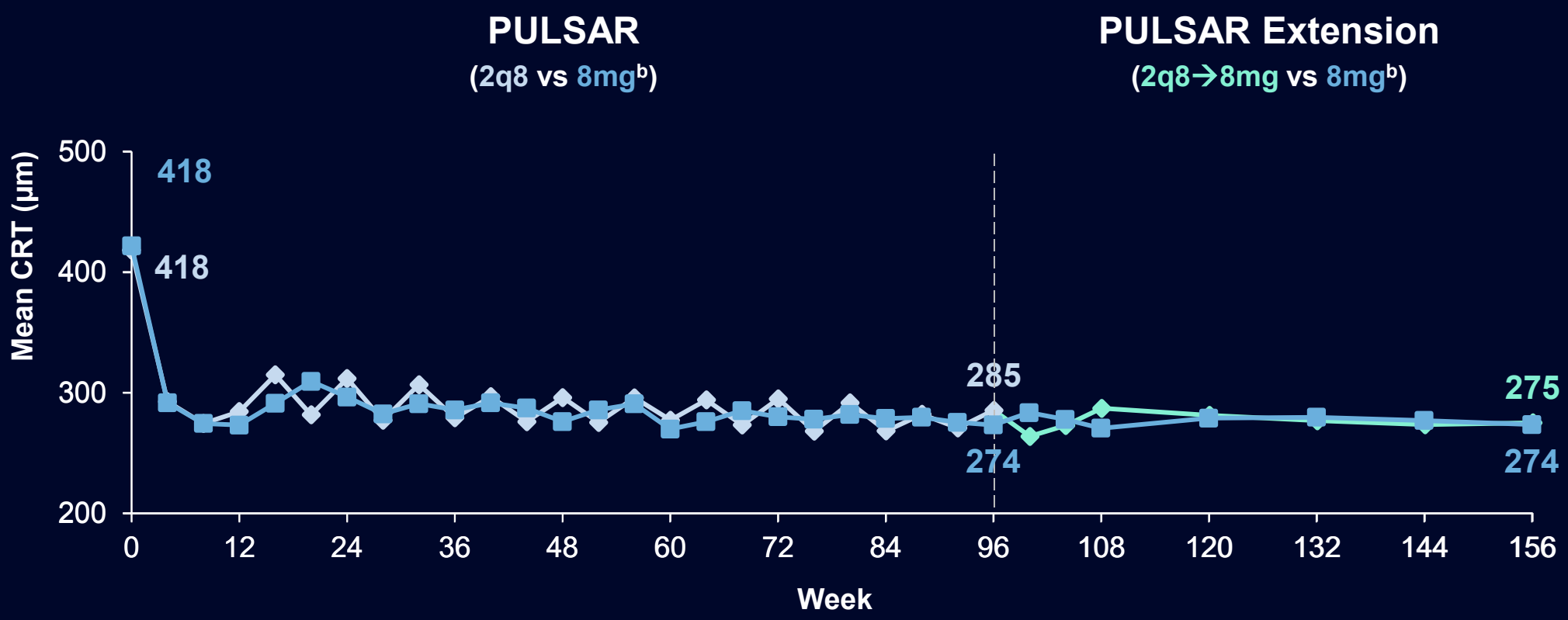

Note: At Week 156, the 2q8→8mg group (n=208) and 8mg group (n=417) reported LS mean (95% CI) changes from baseline (MMRM) in CRT of −145 (−155, −136) µm and −148 (−156, −140) µm, respectively. MMRM was used to generate CRT LS means for the eFAS with baseline CRT as a covariate; treatment group (aflibercept 8q12, 8q16, 2q8), visit, and stratification variables (geographic region [Japan vs rest of the world] and baseline BCVA [<60 vs ≥60 letters]) as fixed factors; and terms for the interaction between visit and baseline CRT and the interaction between visit and treatment. [a]eFAS (observed cases). [b]Patients who were randomly assigned to the 8q12 or 8q16 groups at the beginning of the PULSAR study and continued treatment with aflibercept 8 mg through the PULSAR Extension. [c]eSAF (156-week completers; 2q8→8mg, n=186; 8q12, n=185; 8q16, n=190; 8mg, n=375).

Dosing Intervals Through Week 156

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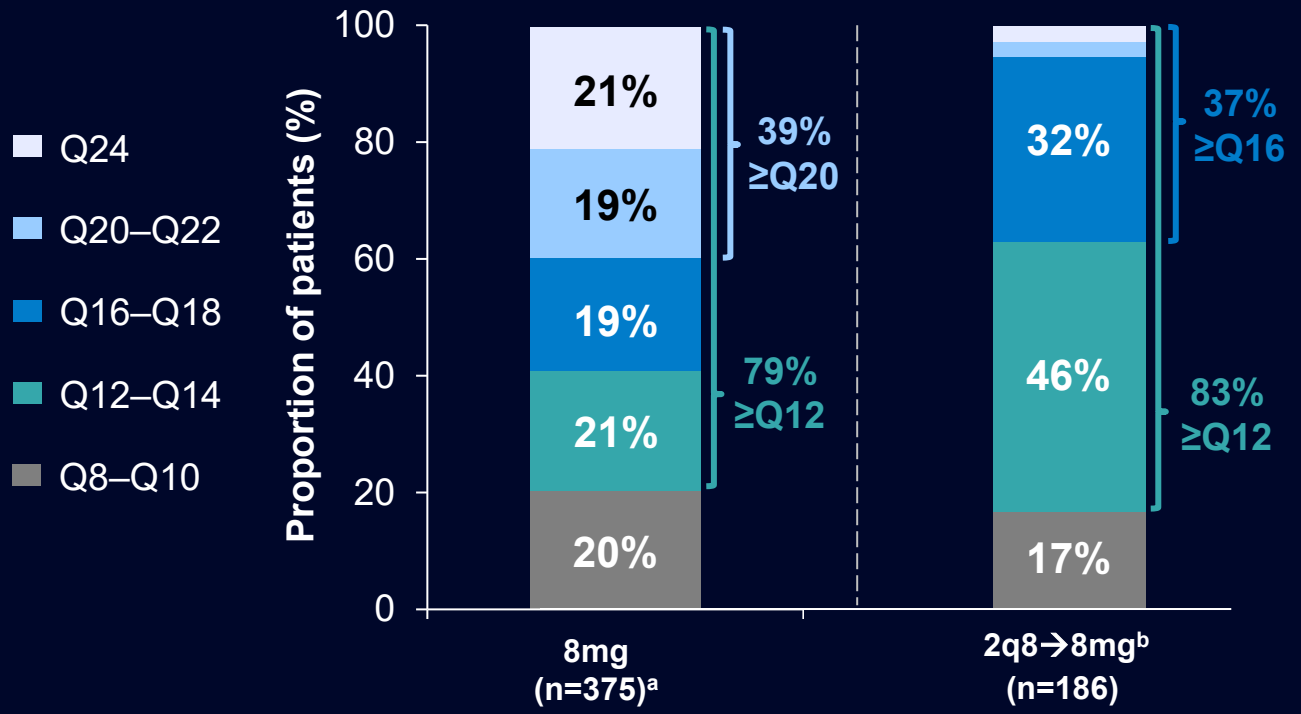
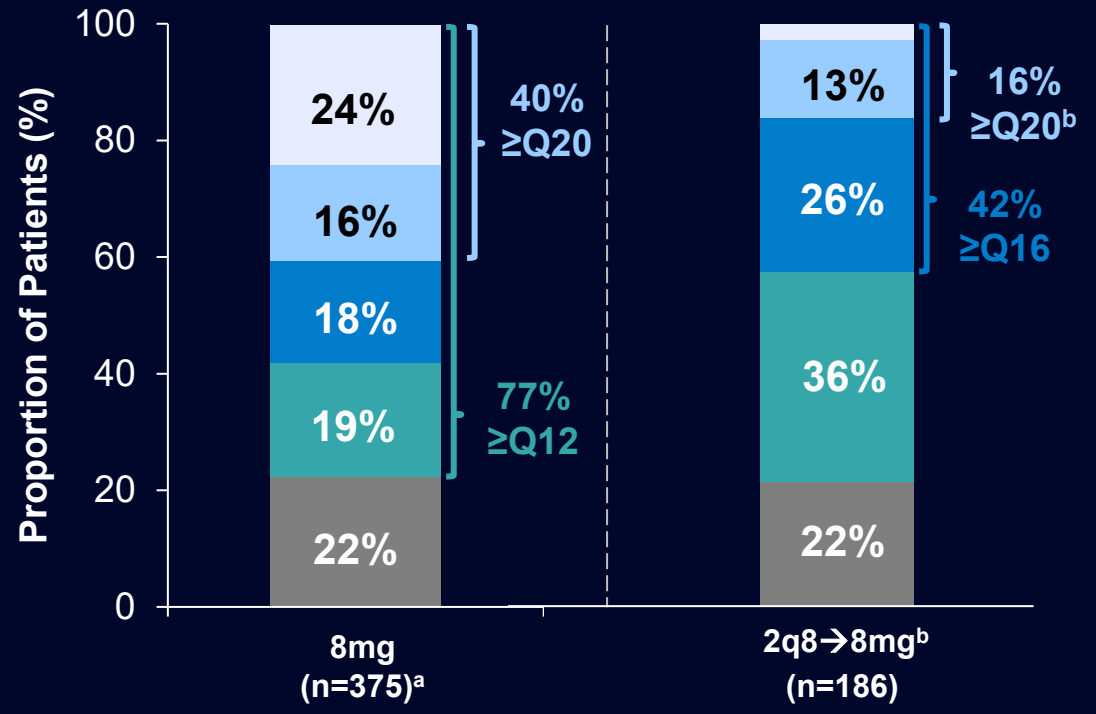
Last Completed Dosing Interval



Last Assigned Dosing Interval



eSAF, patients completing Week 156. Values may not add up to 100% due to rounding. [a]One patient had a missing value for this assessment. [b]Per protocol, patients in the 2q8→8mg group did not have sufficient time to achieve a last assigned dosing interval of >Q20 by Week 156; patients misassigned to longer dosing intervals are included here for completeness. Q8, every 8 weeks; Q10, every 10 weeks; Q12, every 12 weeks; Q14, every 14 weeks; Q16, every 16 weeks; Q18, every 18 weeks, Q20, every 20 weeks; Q22, every 22 weeks; Q24, every 24 weeks.

Reduction in CNV[a] Lesion Area Through Week 156

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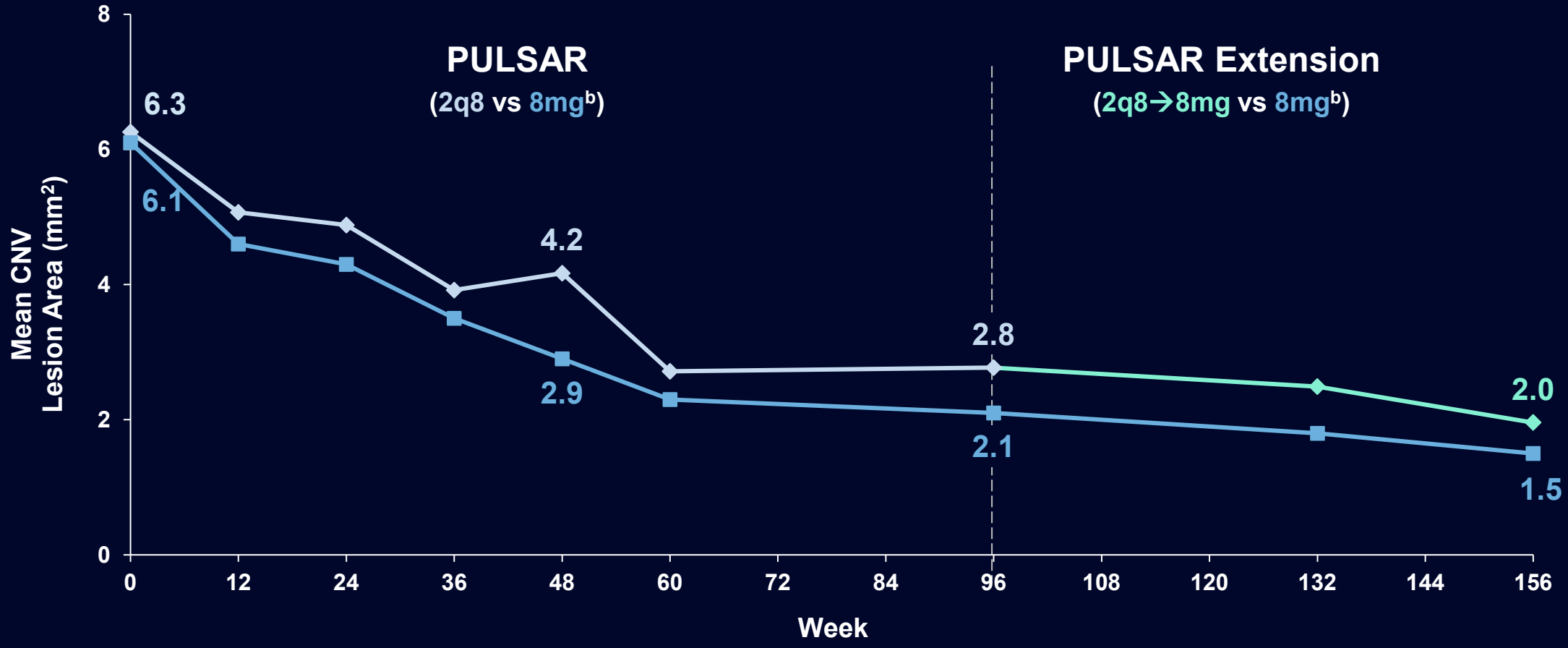

[a]eFAS (observed cases) based on fluorescein angiography/fundus photography assessment. [b]Patients who were randomly assigned to the 8q12 or 8q16 groups at the beginning of the PULSAR study and continued treatment with aflibercept 8 mg through the PULSAR Extension. **CNV**, choroidal neovascularization.

Ocular and Non-Ocular Safety From Main Baseline Through Week 156

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	2q8→8mg	8mg	Total
N (eSAF)	208	417	625
Ocular TEAEs, n (%)[a]	130 (62.5)	251 (60.2)	381 (61.0)
Ocular SAEs, n (%)[a]	7(3.4)	21 (5.0)	28 (4.5)
Intraocular inflammation, n (%)[a]	5 (2.4)	8 (1.9)	13 (2.1)
Non-ocular SAEs, n (%)	43 (20.7)	106 (25.4)	149 (23.8)
APTC events, n (%)	4 (1.9)	7 (1.7)	11 (1.8)
Deaths, n (%)	4 (1.9)	9 (2.2)	13 (2.1)

- Ocular TEAEs reported in ≥4% of all patients included cataract, retinal hemorrhage, reduced visual acuity, vitreous floaters, and increased intraocular pressure
- No cases of occlusive vasculitis were reported

[a]Cumulative events in the study eye from the main PULSAR study baseline through Week 156.
APTC, Anti-Platelet Trialists' Collaboration; **SAE**, serious adverse event; **TEAE**, treatment-emergent adverse event.

PULSAR Extension: Key Week 156 Results

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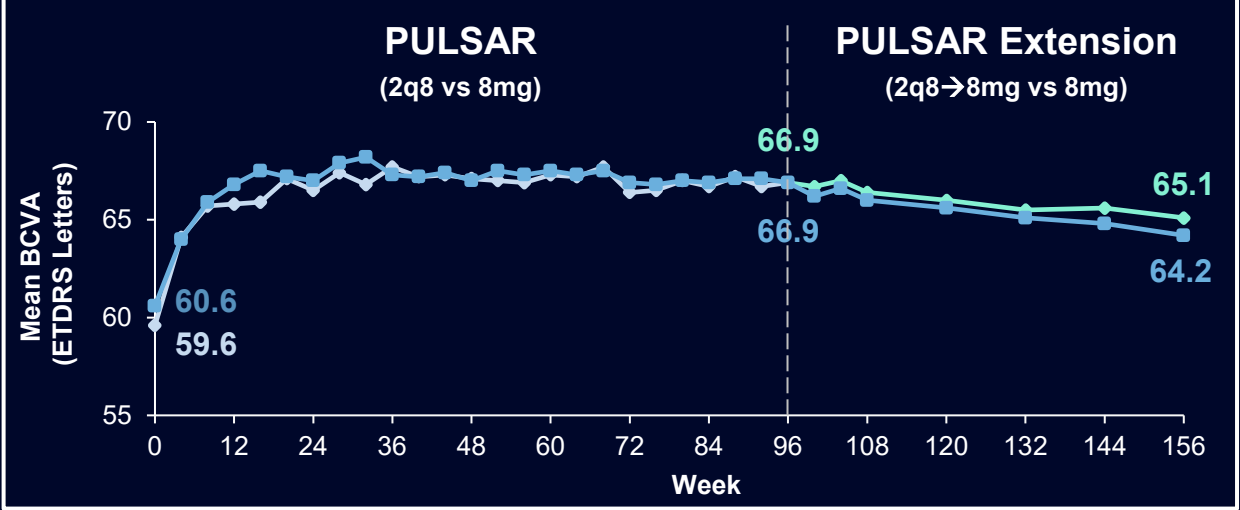
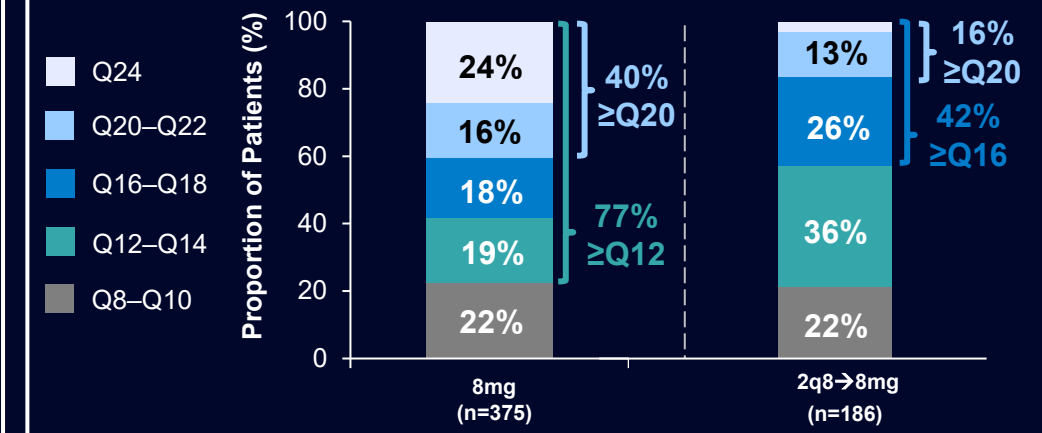
- In the PULSAR Extension, functional and anatomic improvements were sustained through Week 156 in the **2q8→8mg and 8mg groups**
- Mean BCVA and CRT were comparable at Week 156 between the **2q8→8mg and 8mg groups**
  - Patients in the **2q8→8mg group** achieved these improvements with **extended dosing intervals** and a **mean of 4.7 injections** from Week 96 through Week 156
- The majority of patients achieved extended dosing intervals at Week 156
- These findings suggest that patients with treatment-naïve nAMD can achieve **durable improvements with aflibercept 8 mg** administered over extended dosing intervals
- The safety profile of aflibercept 8 mg was comparable to that of aflibercept 2 mg

Mean BCVA Through Week 156[a]



Last Assigned Dosing interval at Week 156[b]



[a]eFAS, OC. [b]eSAF, patients completing Week 156. **OC**, observed cases.