Comparable Efficacy and Safety with Aflibercept 8 mg at Extended Dosing Intervals Beyond q16 Versus 2 mg q8 in Asian Patients with nAMD in PULSAR Through Week 96

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Disclosures

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PULSAR: Multicenter, Randomized, Double-masked Study

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Patients with treatment-naïve nAMD

2q8	8q12	8q16
n=336	n=335	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 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 after 3 initial monthly injections; **8q12**, aflibercept 8 mg every 12 weeks after 3 initial monthly injections; **8q16**, aflibercept 8 mg every 16 weeks after 3 initial monthly injections; **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.

PULSAR Asian Subgroup: Baseline Demographics and Disease Characteristics

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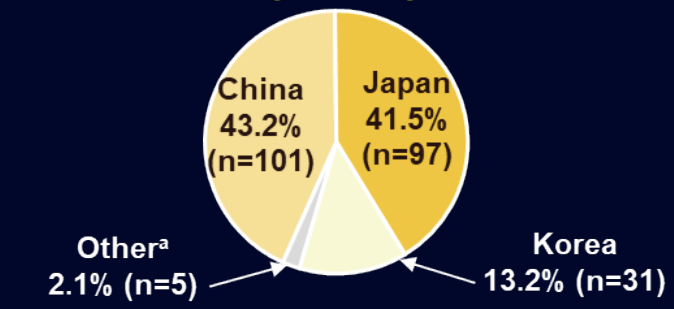
- PULSAR is a global study conducted across 223 sites in 27 countries
- 234 Asian patients were identified by race from the overall population
- Outcomes in the Asian subgroup were analyzed post hoc

Asian Patients by Country of Enrolment



BL demographics and disease characteristics	Asian Subgroup				Overall Population			
	2q8	8q12	8q16	All 8 mg	2q8	8q12	8q16	All 8 mg
	n=83	n=74	n=77	n=151	n=336	n=335	n=338	n=673
Age, years	70.7 (8.9)	71.5 (7.3)	71.6 (8.1)	71.5 (7.7)	74.2 (8.8)	74.7 (7.9)	74.5 (8.5)	74.6 (8.2)
Female, %	31.3	35.1	23.4	29.1	56.0	54.3	53.3	53.8
BCVA, ETDRS letters	59.2 (14.1)	57.7 (13.9)	58.1 (12.2)	57.9 (13.0)	58.9 (14.0)	59.9 (13.4)	60.0 (12.4)	59.9 (12.9)
CRT, µm	365 (149)	366 (128)	347 (131)	356 (130)	367 (134)	370 (124)	371 (133)	371 (128)
CNV size, mm^2	5.4 (4.6)	5.7 (4.9)	6.0 (5.1)	5.9 (5.0)	6.4 (5.0)	6.0 (4.8)	6.5 (5.5)	6.3 (5.2)
CNV type, %								
Minimally classic	24.1	24.3	22.1	23.2	18.5	17.0	20.4	18.7
Occult only	56.6	56.8	54.5	55.6	58.3	60.3	55.9	58.1
Predominantly classic	15.7	14.9	14.3	14.6	21.1	21.2	19.8	20.5
PCV (confirmed by ICGA), %[b]	48.2	39.2	36.4	37.7	16.1	13.1	12.1	12.6

FAS. Data are mean (SD) unless otherwise indicated.
[a]Other comprised USA (n=2), Australia (n=2), and Singapore (n=1).
[b]ICGA was not performed for all patients (assessments were not available for up to 32% of patients); as such, the actual percentages of PCV may be higher than reported here.
BL, baseline; **CNV**, choroidal neovascularization; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **FAS**, full analysis set; **ICGA,** indocyanine green angiography; **PCV**, polypoidal choroidal vasculopathy; **SD**, standard deviation.

BCVA Outcomes Through Week 96: Comparable Between Aflibercept 8 mg and 2 mg

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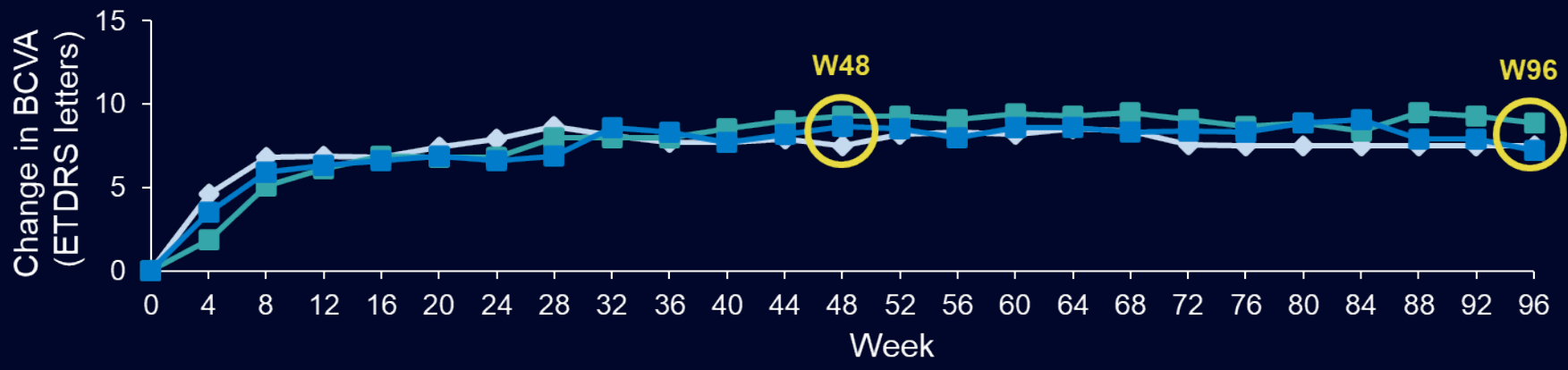
Asian Subgroup



	W48	W96
2q8 (n=83)[a]	+7.5	+7.5
8q12 (n=74)[a]	+9.3	+8.9
8q16 (n=77)[a]	+8.8	+7.2

		W48			W96		
		Absolute BCVA	Change from BL	Two-sided 95% CI	Absolute BCVA	Change from BL	Two-sided 95% CI
Asian subgroup	2q8 (n=83)[a]	66.7 ± 16.6	+7.5 ± 12.9	4.7, 10.3	66.7 ± 15.4	+7.5 ± 12.5	4.8, 10.3
	8q12 (n=74)[a]	67.0 ± 16.9	+9.3 ± 15.4	5.7, 12.9	66.6 ± 18.1	+8.9 ± 16.6	5.1, 12.8
	8q16 (n=77)[a]	66.9 ± 14.0	+8.8 ± 9.0	6.8, 10.8	65.3 ± 14.7	+7.2 ± 10.5	4.8, 9.6
Overall population	2q8 (n=336)[a]	66.5 ± 16.2	+7.5 ± 12.0	6.2, 8.8	66.1 ± 16.3	+7.1 ± 13.0	5.7, 8.5
	8q12 (n=335)[a]	66.0 ± 16.4	+6.1 ± 13.2	4.7, 7.6	65.4 ± 17.3	+5.5 ± 14.9	3.9, 7.1
	8q16 (n=338)[a]	66.0 ± 15.6	+5.9 ± 11.8	4.7, 7.2	65.4 ± 16.7	+5.4 ± 13.3	4.0, 6.8

FAS, LOCF (last available observed value prior to ICE was used to impute missing data; ICE were handled according to sensitivity estimand strategy for continuous endpoints). Data are mean ± SD unless otherwise indicated.

[a]N values represent number of patients at baseline.

CI, confidence interval; **ICE,** intercurrent event; **LOCF,** last observation carried forward.

Absolute and Change in CRT Through Week 96: Comparable Between Aflibercept 8 mg and 2 mg

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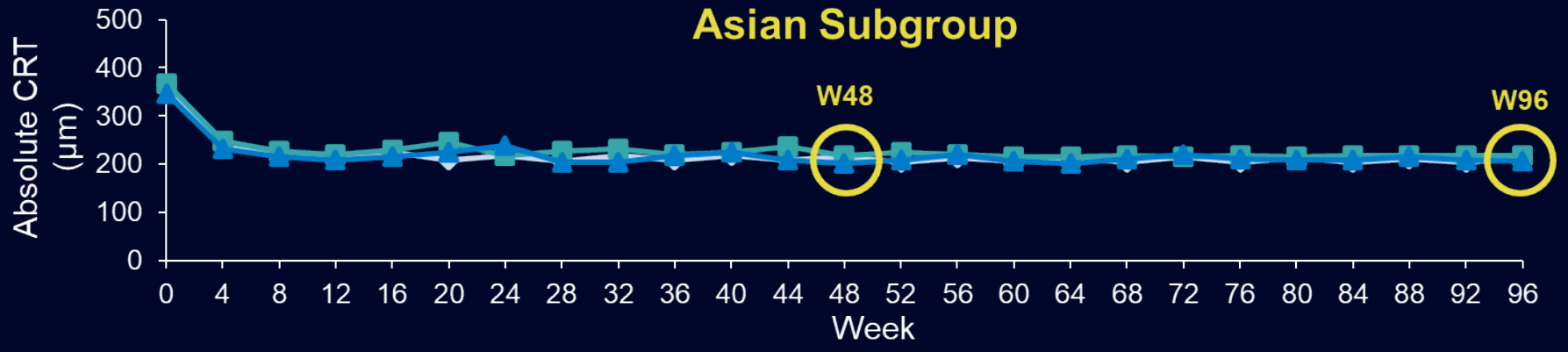
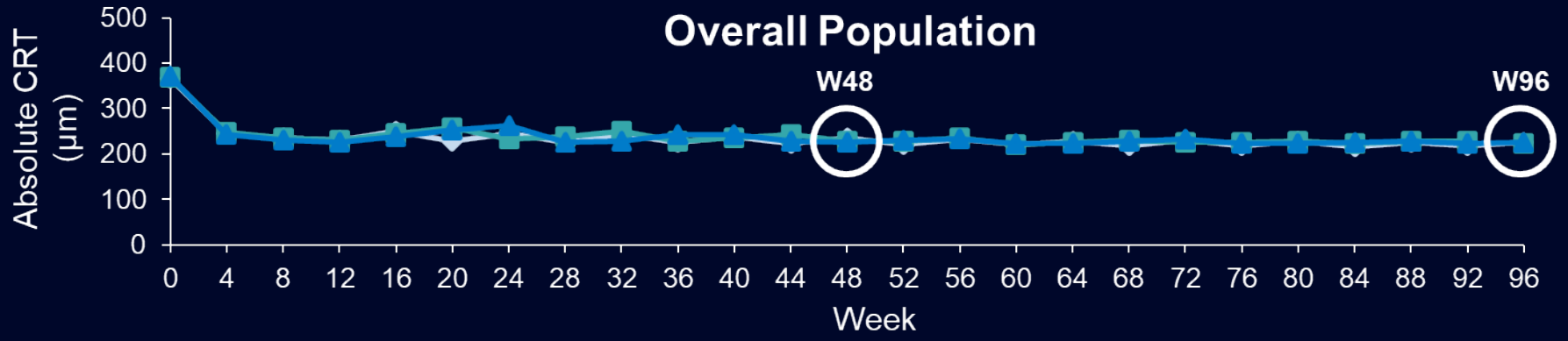
Asian Subgroup



	W48	W96
2q8 (n=82)[a]	−139	−144
8q12 (n=74)[a]	−148	−147
8q16 (n=77)[a]	−147	−140

Overall Population



	W48	W96
2q8 (n=335)[a]	−130	−141
8q12 (n=335)[a]	−141	−147
8q16 (n=336)[a]	−143	−145

	Asian Subgroup			Overall Population	
	Mean ± SD change from BL to Week 96 (LOCF)	Two-sided 95% CI		Mean ± SD change from BL to Week 96 (LOCF)	Two-sided 95% CI
2q8 (n=83)[a]	−144 ± 146	−176, −111	2q8 (n=335)[a]	−141 ± 132	−155, −126
8q12 (n=74)[a]	−147 ± 137	−179, −115	8q12 (n=335)[a]	−147 ± 128	−161, −133
8q16 (n=77)[a]	−140 ± 125	−167, −112	8q16 (n=336)[a]	−145 ± 135	−160, −131

FAS, LOCF (last available observed value prior to ICE was used to impute missing data; ICE were handled according to sensitivity estimand strategy for continuous endpoints).
[a]N values represent number of patients with CRT assessments at baseline.

Fluid Control Achieved at Week 16 Sustained Through Week 96 for Aflibercept 8 mg and 2 mg

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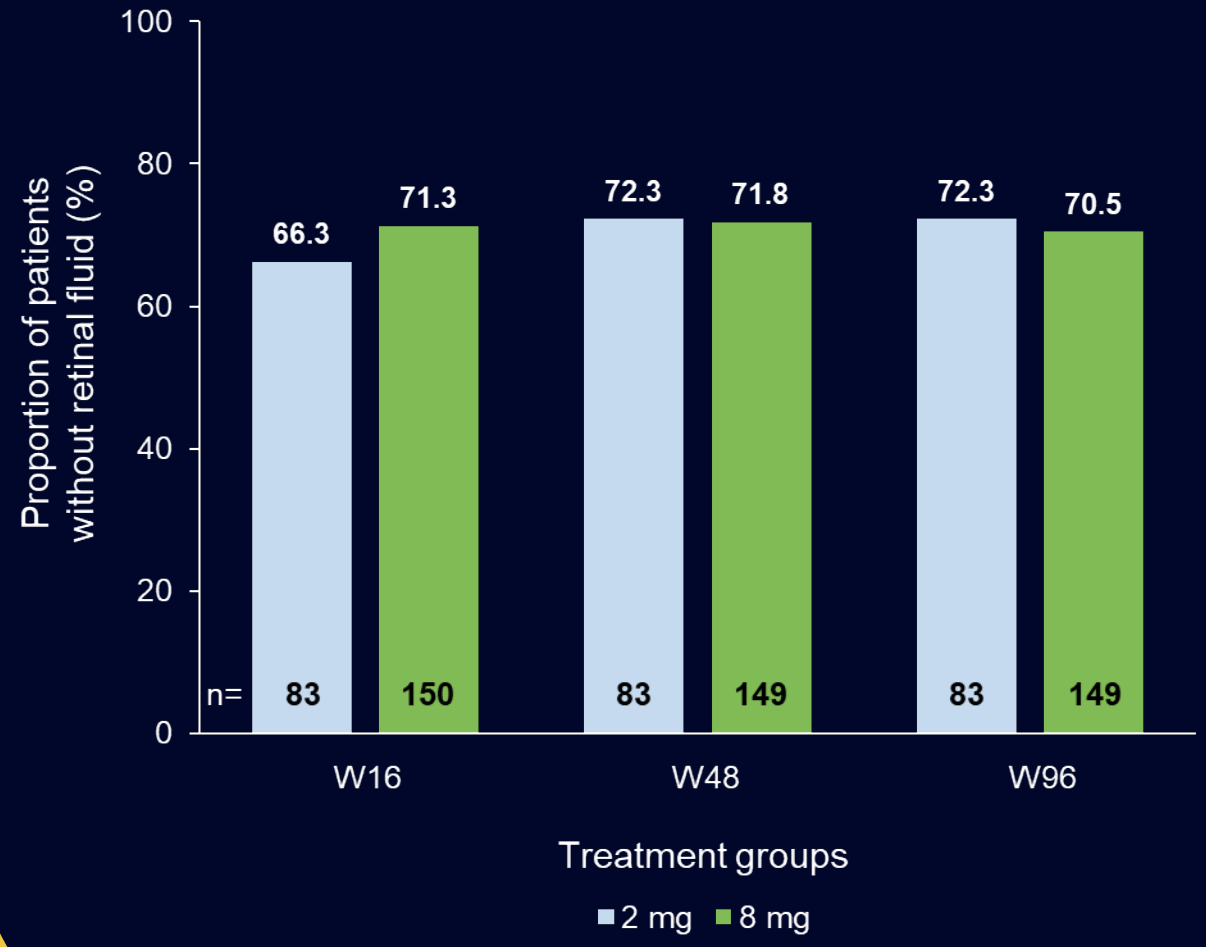
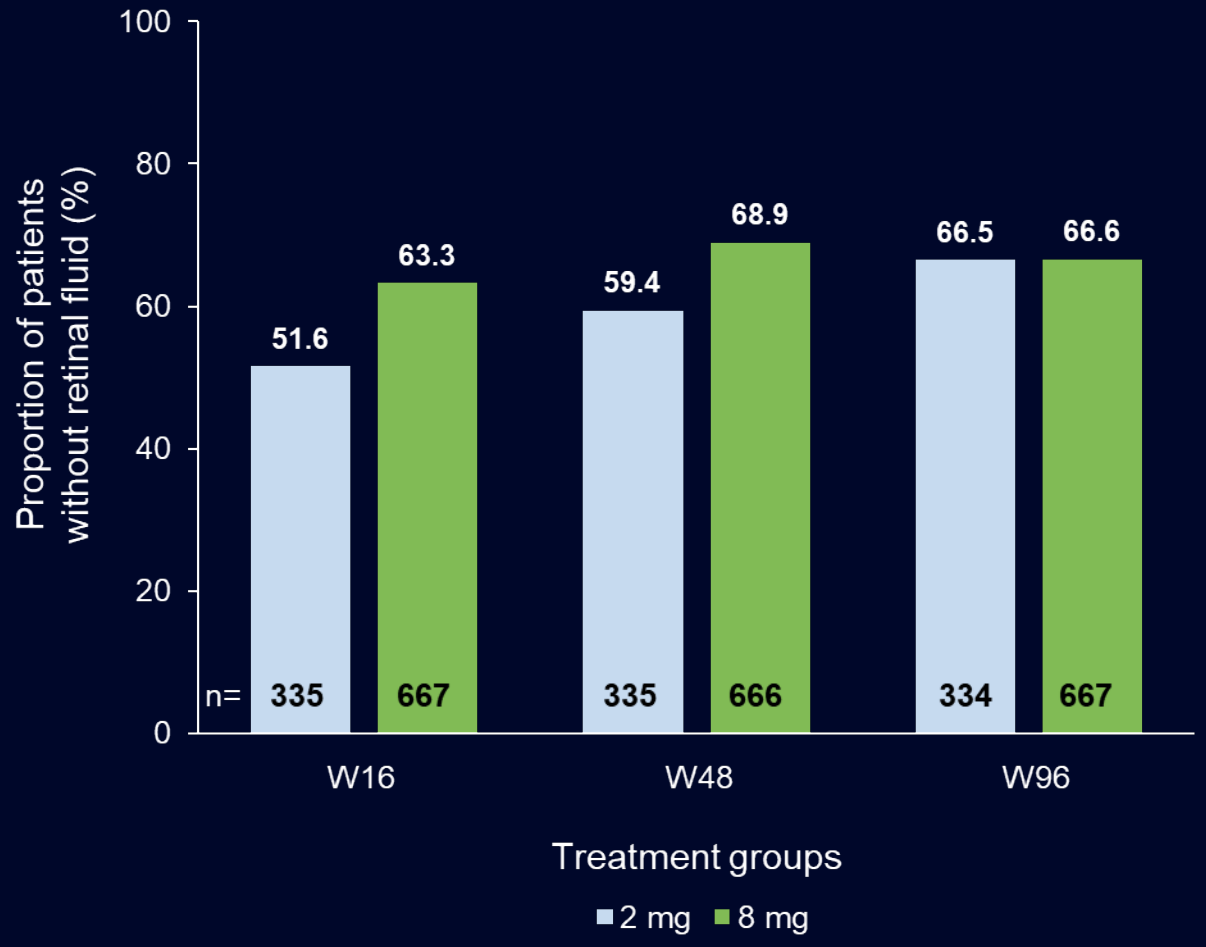
Asian Subgroup



Overall Population



FAS, LOCF (data post ICE were censored). "Without retinal fluid" is defined as absence of intraretinal and subretinal fluid in the center subfield.

Most Asian Patients Receiving Aflibercept 8 mg Qualified for an Extended Dosing Interval at Week 96[a]

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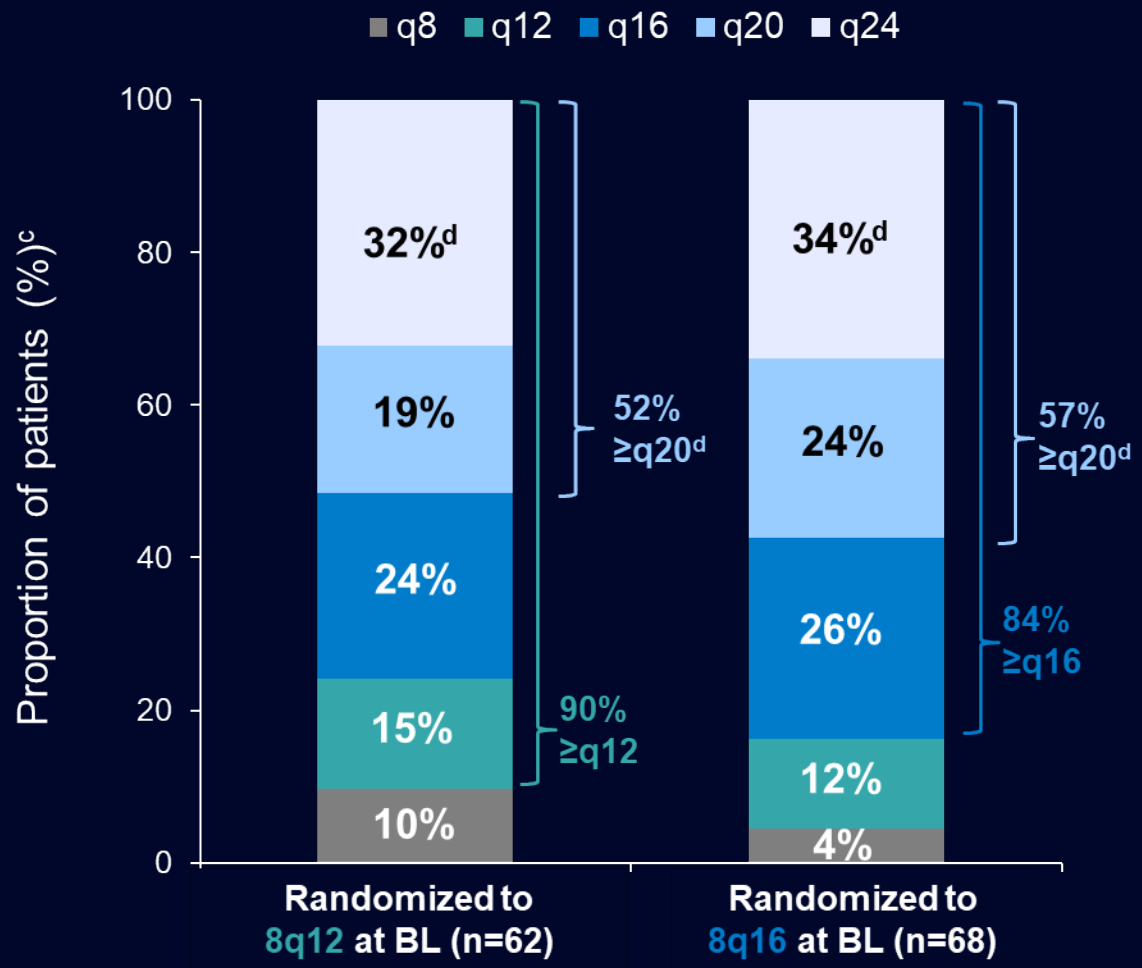
Last Assigned Dosing Interval (Asian Subgroup)[a,b,c]



Mean Number of Injections for the Asian Subgroup

	Weeks 0–48[e]	Weeks 0–96[b]
2q8	6.8	12.6
8q12	5.7	9.4
8q16	4.8	7.8

[a]Dosing intervals were extended in Year 2 if patients had <5-letter loss in BCVA from Week 12 **AND** no fluid at the center subfield **AND** no new foveal hemorrhage or neovascularization.
[b]Patients completing Week 96. Asian subgroup: 2q8 n=69, 8q12 n=62, 8q16 n=68. [c]Values may not add up due to rounding. [d]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period. [e]Patients completing Week 48. Asian subgroup: 2q8 n=74, 8q12 n=66, 8q16 n=71.

96-Week Ocular Safety Profile of Aflibercept 8 mg: Similar to 2 mg in Asian and Overall Populations

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TEAEs in the study eye, n (%)	Asian Subgroup				Overall Population			
	2q8	8q12	8q16	All 8 mg	2q8	8q12	8q16	All 8 mg
	n=83	n=74	n=77	n=151	n=336	n=335	n=338	n=673
Any ocular TEAE	40 (48.2)	33 (44.6)	39 (50.6)	72 (47.7)	181 (53.9)	171 (51.0)	174 (51.5)	345 (51.3)
Any IOI TEAE	2 (2.4)	1 (1.4)	0	1 (0.7)	7 (2.1)	6 (1.8)	3 (0.9)	9 (1.3)

- Ocular TEAEs occurring in ≥5% of patients in any treatment arm in the Asian subgroup were increased intraocular pressure, retinal hemorrhage, cataract, conjunctival hemorrhage, dry eye, reduced visual acuity, and conjunctivitis
- Three cases of IOI occurred in the Asian subgroup: eye inflammation, iritis, and endophthalmitis; none were considered serious, and all were mild or moderate in severity

Data are from the safety analysis set.
IOI, intraocular inflammation, **TEAE**, treatment-emergent adverse event.

Conclusions: Aflibercept 8 mg in Asian Patients

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Efficacy of aflibercept 8 mg largely maintained at Week 96 with fewer injections versus 2 mg	• In the Asian subgroup, robust and stabilized **gains in visual acuity** were observed across all treatment arms from baseline to **Week 48** and **were maintained** through **Week 96** • Robust and comparable **decreases in CRT** from baseline were observed in Asian patients for all 3 treatment arms at **Week 48**, with minimal fluctuations through **Week 96**
Maintenance of fluid control through Week 96	• Fluid control achieved at **Week 16** was **sustained through Week 96** in the Asian subgroup across all treatment regimens • The **proportion of patients** without retinal fluid in the Asian subgroup was **comparable for aflibercept 8 mg versus 2 mg** at **Week 96**
Extended durability of aflibercept 8 mg at Week 96	• At Week 96, **57% of Asian patients** randomly assigned to aflibercept 8q16 qualified for **extension of the dosing interval** to **≥20 weeks**, suggesting extended durability of aflibercept 8 mg versus 2 mg
Comparable safety profile for aflibercept 8 mg versus 2 mg	• The **safety profile of aflibercept 8 mg** in Asian patients was **similar to** that of **aflibercept 2 mg** and to the overall PULSAR population