Intravitreal Aflibercept 8 mg Injection in Patients with Neovascular Age-Related Macular Degeneration: 48- and 96-Week Results from Asian Patients in the Phase 3 PULSAR Trial

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Presented at the 39th Asia-Pacific Academy of Ophthalmology (APAO) Congress, Bali, Indonesia, February 22–25, 2024

Disclosures

- **SJC:** Consultant fees from Bayer, Roche; lecture fees from Alcon, Novartis, Bausch & Lomb
  - **XZ and SL:** Employees of Bayer Consumer Care AG
    AS and TM: Employees of Bayer AG
    MZ: Employee of Bayer Healthcare

- 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)

PULSAR: Multicenter, Randomized, Double-masked Study

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Patients with treatment-naïve nAMD

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.
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.

PULSAR: Asian Subgroup

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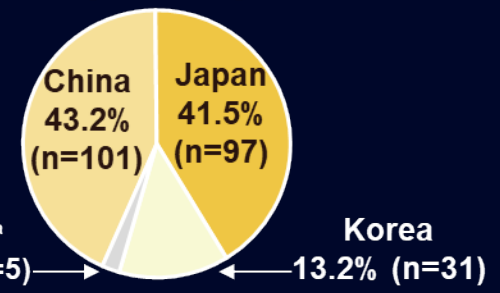
- PULSAR is a global study conducted across 223 sites in 27 countries
- 234 Asian patients were identified by race from the overall population
- Outcomes in this subgroup were analyzed post hoc

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)
CST, 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)
PCV (confirmed by ICGA), %	48.2	39.2	36.4	37.7	16.1	13.1	12.1	12.6

[a]Other comprised USA (n=2), Australia (n=2) and Singapore (n=1).
FAS. Data are mean (SD) unless otherwise indicated.
BL, baseline; **CNV**, choroidal neovascularization; **CST**, central subfield thickness; **ETDRS,** Early Treatment Diabetic Retinopathy Study; **FAS**, full analysis set; **ICGA,** indocyanine green angiography.

Change in BCVA through Week 96: Comparable Gains Observed with Aflibercept 8 mg and 2 mg

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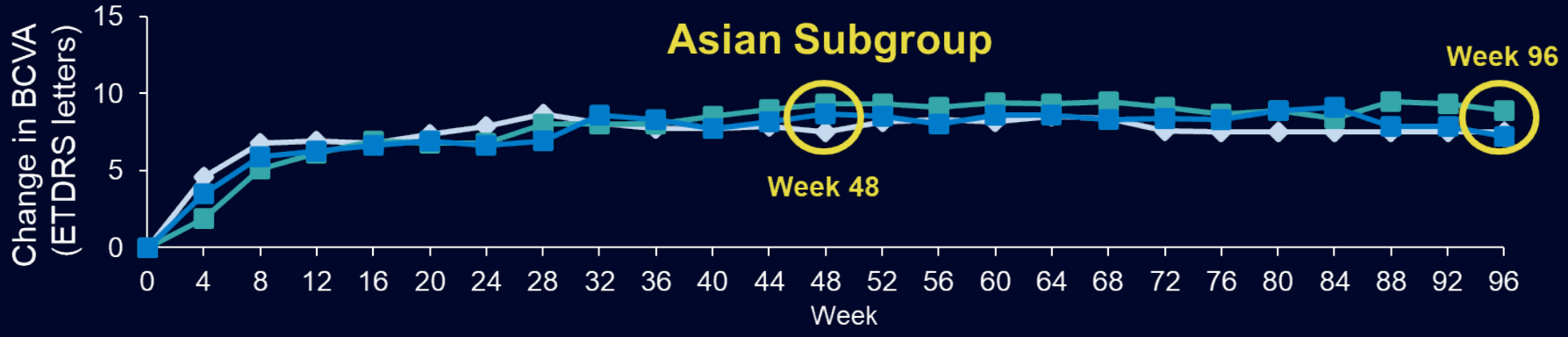
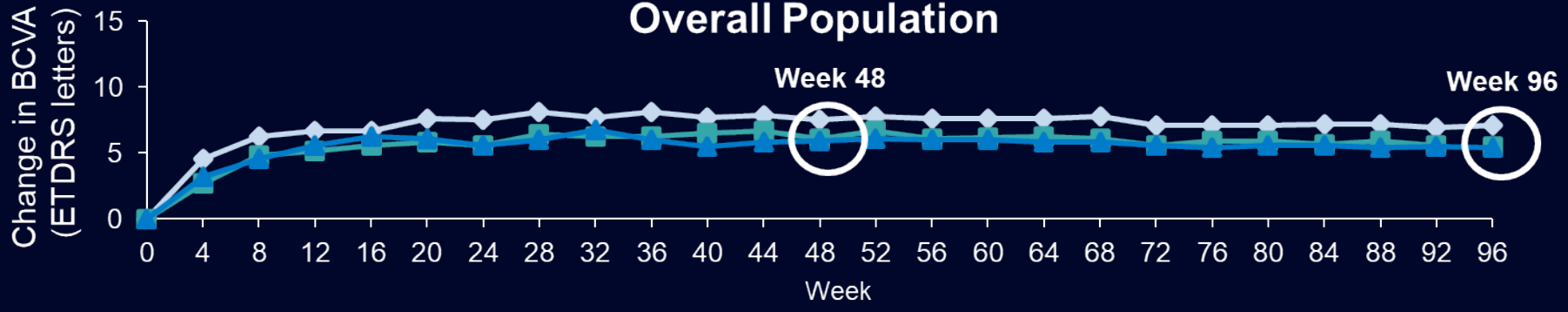


	Week 48	Week 96
2q8 (n=83)[a]	+7.5	+7.5
8q12 (n=74)[a]	+9.3	+8.9
8q16 (n=77)[a]	+8.8	+7.2



	Week 48	Week 96
2q8 (n=336)[a]	+7.5	+7.1
8q12 (n=335)[a]	+6.1	+5.5
8q16 (n=338)[a]	+5.9	+5.4

	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	+7.5 ± 12.5	4.8, 10.3	2q8	+7.1 ± 13.0	5.7, 8.5
8q12	+8.9 ± 16.6	5.1, 12.8	8q12	+5.5 ± 14.9	3.9, 7.1
8q16	+7.2 ± 10.5	4.8, 9.6	8q16	+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).
[a]N values represent number of patients at baseline.
ICE, intercurrent event; **LOCF,** last observation carried forward.

CST Through Week 96: Similar with Aflibercept 8 mg and 2 mg

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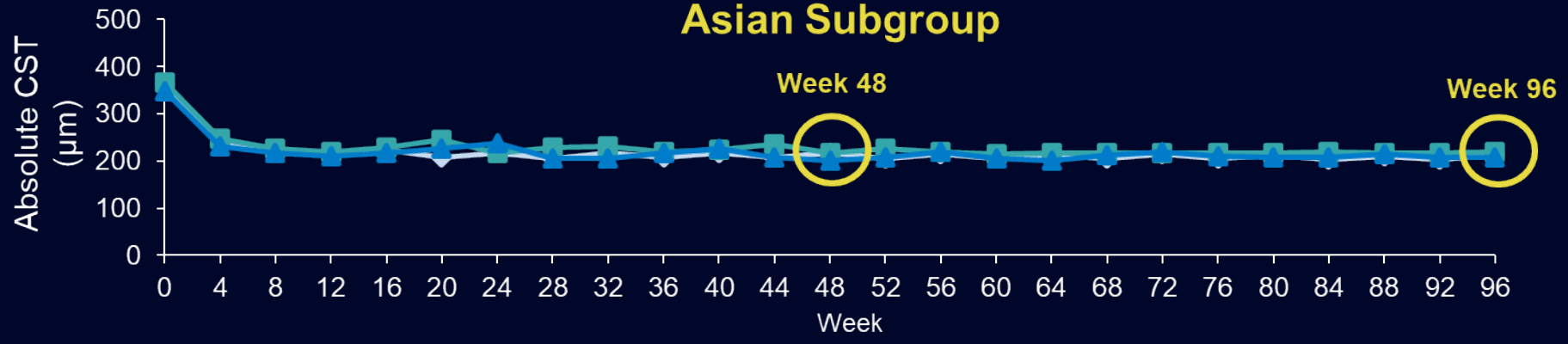
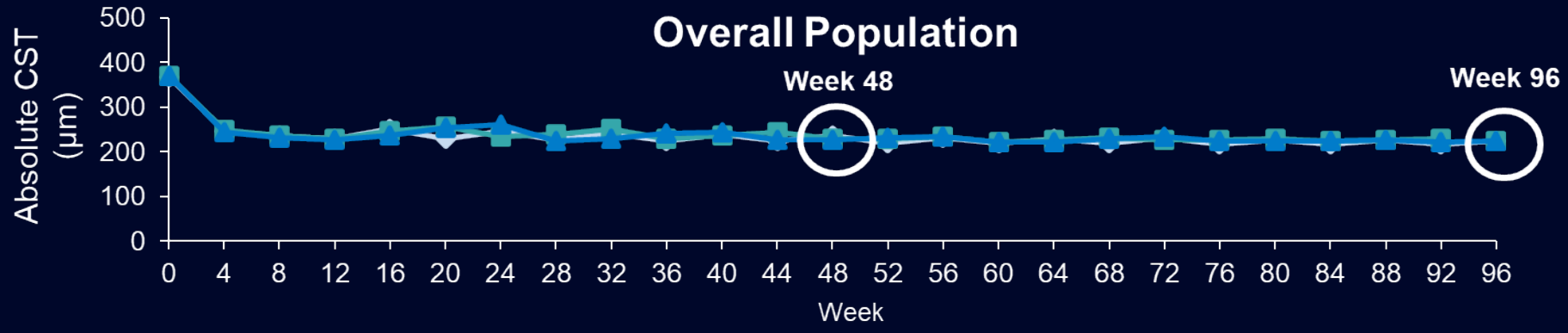
Asian Subgroup



	Week 48	Week 96
2q8 (n=83)[a]	216	212
8q12 (n=74)[a]	217	218
8q16 (n=77)[a]	201	207

Overall Population



	Week 48	Week 96
2q8 (n=335)[a]	236	225
8q12 (n=335)[a]	228	223
8q16 (n=336)[a]	227	225

	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	−144 ± 146	−176, −111	2q8	−141 ± 132	−155, −126
8q12	−147 ± 137	−179, −115	8q12	−147 ± 128	−161, −133
8q16	−140 ± 125	−167, −112	8q16	−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 CST assessments at baseline.
CST, central subfield retinal thickness; **ICE,** intercurrent event; **LOCF,** last observation carried forward.

Most Asian Patients Qualified for an Extended Dosing Interval at Week 96[a]

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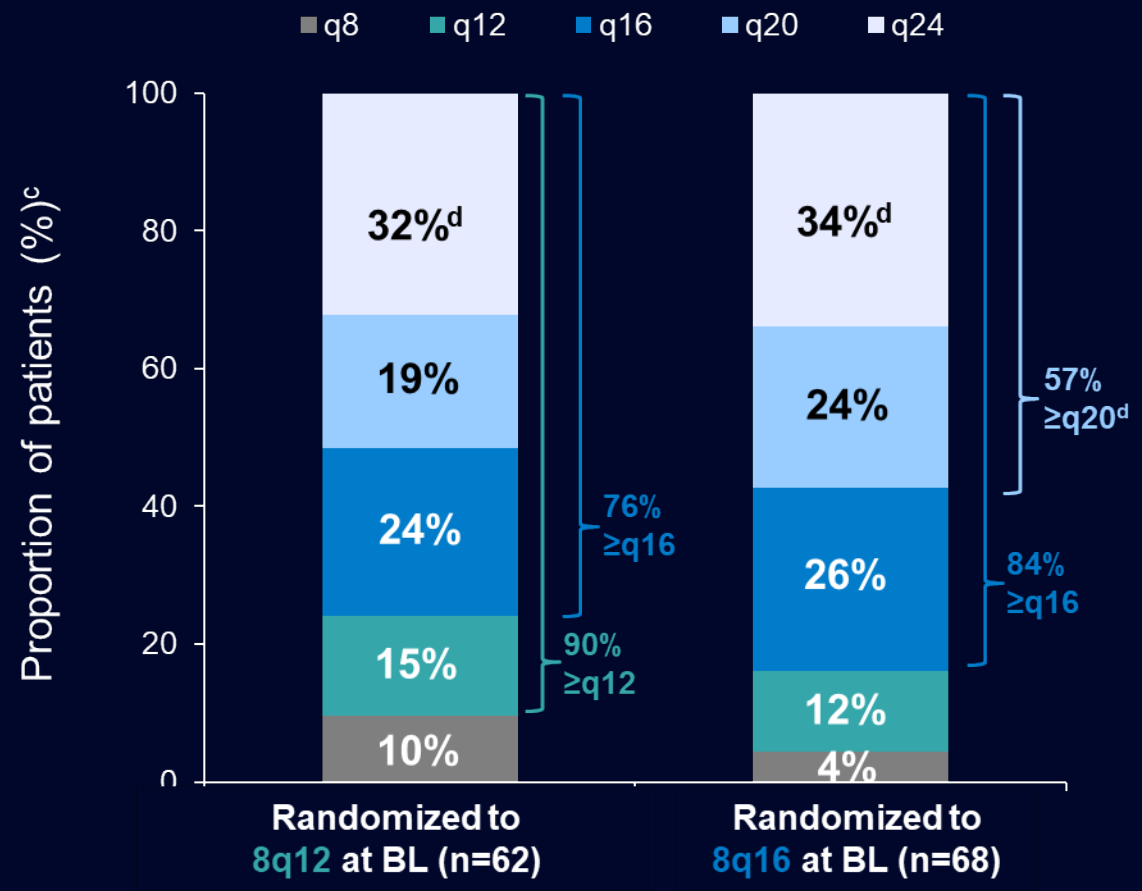
Last Assigned Dosing Interval (Asian Subgroup)[a,b,c]



Mean number of injections for the Asian subgroup

	Weeks 0–48[e]	Weeks 0–96[b]
2q8	6.9	12.6
8q12	6.0	9.4
8q16	5.0	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 central 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.
q12, every 12 weeks; **q16**, every 16 weeks; **q20**, every 20 weeks.

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, %	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 intraocular inflammation 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 intraocular inflammation occurred in the Asian subgroup: eye inflammation (2q8), iritis (8q12) and endophthalmitis (2q8); none were considered serious, and all IOI cases were mild or moderate in severity

Data are from the safety analysis set.
AE, adverse event; **TEAE**, treatment-emergent adverse event.

Conclusions: Aflibercept 8 mg in Asian Patients

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Efficacy of aflibercept 8 mg largely maintained in Asian patients over 2 years

- **Visual acuity gains** from baseline were **largely maintained from Week 48 to Week 96** in the aflibercept 8q12, 8q16, and 2q8 Asian subgroups, with gains of +8.9, +7.2, and +7.5. letters, respectively, from baseline to Week 96
- Through Week 96, the absolute and mean change in **CST** from baseline were numerically **similar** in the 3 treatment arms

Extended durability

Data suggests **extended durability of aflibercept 8 mg versus aflibercept 2 mg**
At Week 96:

- 90% of patients randomized to 8q12 were assigned to dosing intervals of ≥12 weeks
- 84% of patients randomized to 8q16 were assigned to dosing intervals of ≥16 weeks
- 57% patients randomized to 8q16 were assigned to dosing intervals of ≥20 weeks

Comparable safety profile for aflibercept 8 mg versus 2 mg

- In the PULSAR study, the **safety profile of aflibercept 8** mg was **similar to that of aflibercept 2 mg** in the Asian subgroup and overall study population