



PULSAR Extension: Anatomic Control and Extended Dosing Intervals with Aflibercept 8 mg in Patients with Neovascular Age-related Macular Degeneration Who Switched from Aflibercept 2 mg

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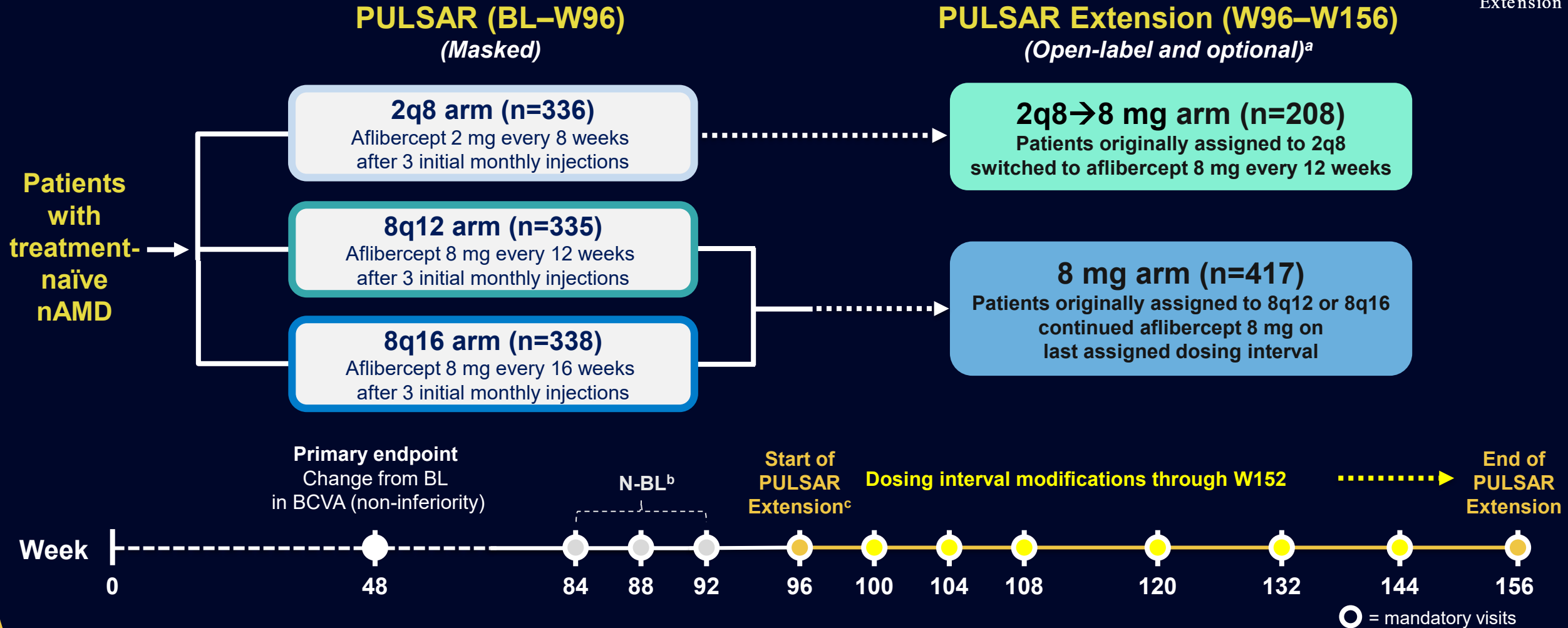
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PULSAR Extension Design



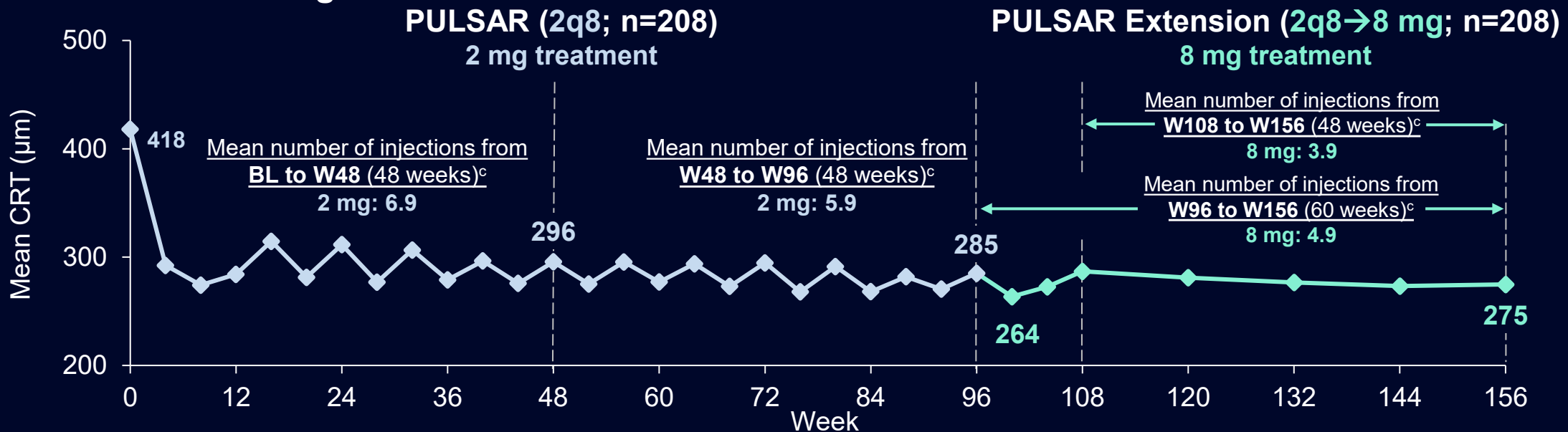
^aTo be eligible for PULSAR Extension, patients had to have ≥1 BCVA and CRT assessments between W84 and W92. Masked transition period (W96–108) was followed by open-label part (W108–W156).

^bN-BL was an average of values from W84, 88, and 92. ^cOptional 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.

Rationale

- This post hoc analysis, based on the CRT quartiles^a and CRT ≥ 300 μm at extension BL (W96), aims to understand the impact of switching from aflibercept 2 mg to 8 mg on visual and anatomic outcomes (including duration of treatment effect) based on the clinical status at the point of switch in patients with:
 - Poor disease control on 2q8 regimen to evaluate clinical benefit after switching
 - Stable disease to assess maintenance of disease control on 8 mg at extended intervals

Mean CRT^b Through W156



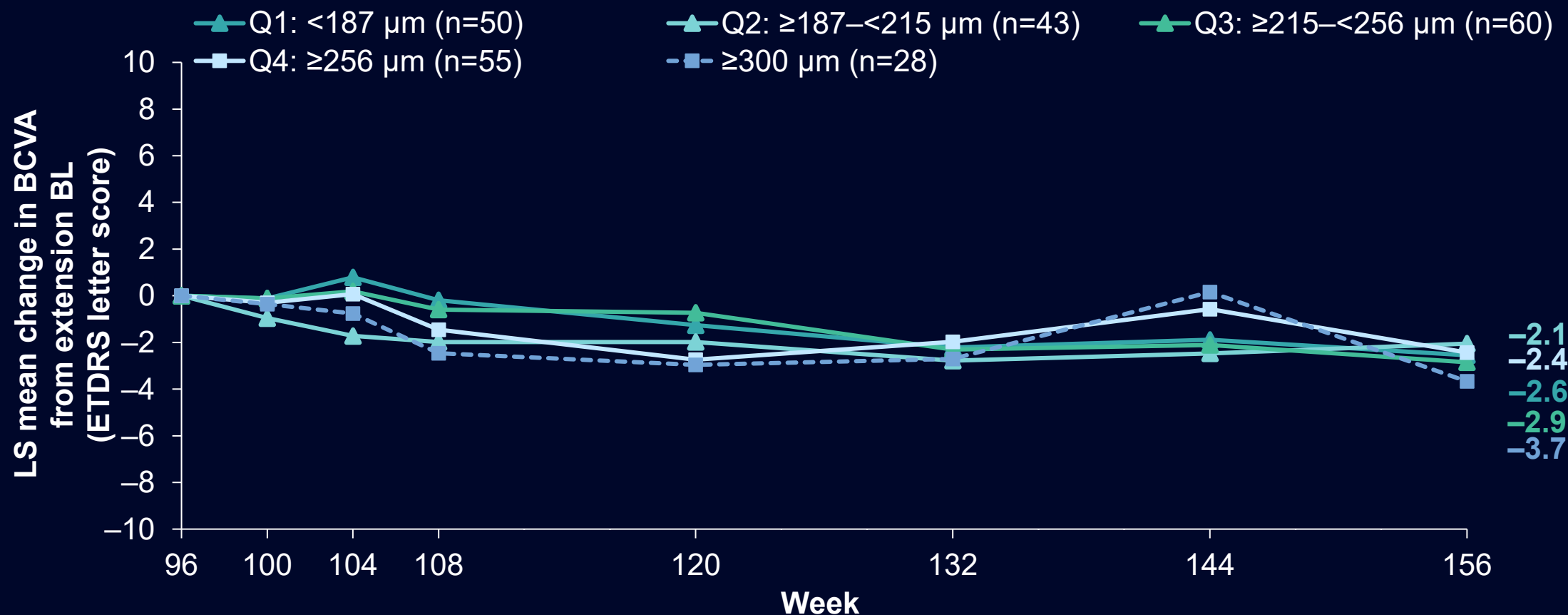
Note: At W156, the 2q8→8mg group (n=208) reported a LS mean (95% CI) change (MMRM)^d from BL in CRT of -145 (-155, -136) μm . ^aQuartiles were defined as: Q1 [<187 μm], Q2 [≥ 187 - <215 μm], Q3 [≥ 215 - <256 μm], and Q4 [≥ 256 μm]. ^beFAS (OC). ^ceSAF. ^dLS means were generated for the eFAS using MMRM with BL CRT as a covariate; treatment group (aflibercept 2q8), visit, and stratification variables (geographic region [Japan vs rest of the world] and BL BCVA [<60 vs ≥ 60 letters]) as fixed factors; and terms for the interaction between visit and BL CRT and the interaction between visit and treatment. CI, confidence interval; eFAS, PULSAR Extension full analysis set; eSAF, safety analysis set in the PULSAR Extension; EXT, Extension; LS, least squares; MMRM, mixed model for repeated measures; OC, observed cases; Q, quartile.

Patient Disposition and BL Characteristics At PULSAR BL (W0) and Extension BL (W96) in W96 CRT Quartiles

	2q8→8mg				
	CRT at PULSAR Extension BL (W96)				
	Q1: <187 μm (n=50)	Q2: ≥ 187 –<215 μm (n=43)	Q3: ≥ 215 –<256 μm (n=60)	Q4: ≥ 256 μm (n=55)	Subgroup of Q4 ≥ 300 μm (n=28)
Age, years	74.7 (9.0)	74.9 (8.4)	73.7 (8.2)	72.6 (7.5)	72.6 (8.3)
Female, %	70.0	55.8	63.3	45.5	53.6
BL (W0)					
BCVA, ETDRS letters	51.1 (15.3)	58.9 (12.9)	66.4 (10.1)	60.4 (12.3)	56.6 (13.1)
CRT, μm^{a}	356 (148)	351 (95)	338 (101)	413 (182)	472 (219)
Extension BL (W96)					
BCVA, ETDRS letters	54.8 (18.8)	67.8 (17.2)	74.7 (14.4)	68.5 (14.5)	65.4 (17.2)
CRT, μm^{a}	157 (19.6)	202 (7.8)	230 (12.2)	334 (127)	389 (160)

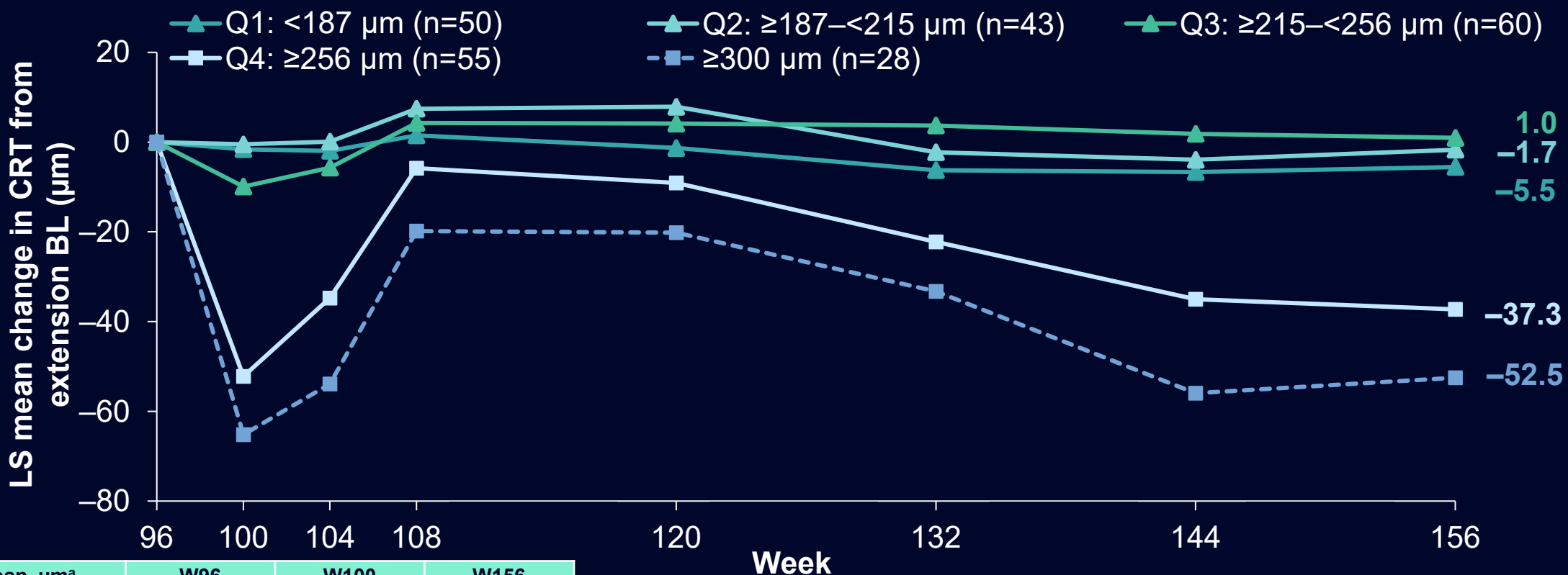
- At extension BL (W96), patients originally assigned to aflibercept 2 mg (BL–W96) switched to aflibercept 8 mg (W96–W156)
- CRT ≥ 300 μm at W96 identifies a subgroup of the Q4 patient cohort with poorer disease control at the point of switch from aflibercept 2q8 to aflibercept 8 mg dosing regimen

BCVA was Generally Maintained Following Switch to Aflibercept 8 mg from 2 mg, with Fewer Injections



MMRM was used with BL BCVA measurement as a covariate, treatment group, visit and the stratification variables (geographic region [Japan vs. Rest of World]; BL BCVA [<60 vs. ≥60]) as fixed factors, and terms for the interaction between BL BCVA and visit and the interaction between treatment and visit. **LS**, least squares.

Subgroups with the Highest CRT Showed a Decrease in CRT After Switching to Aflibercept 8 mg

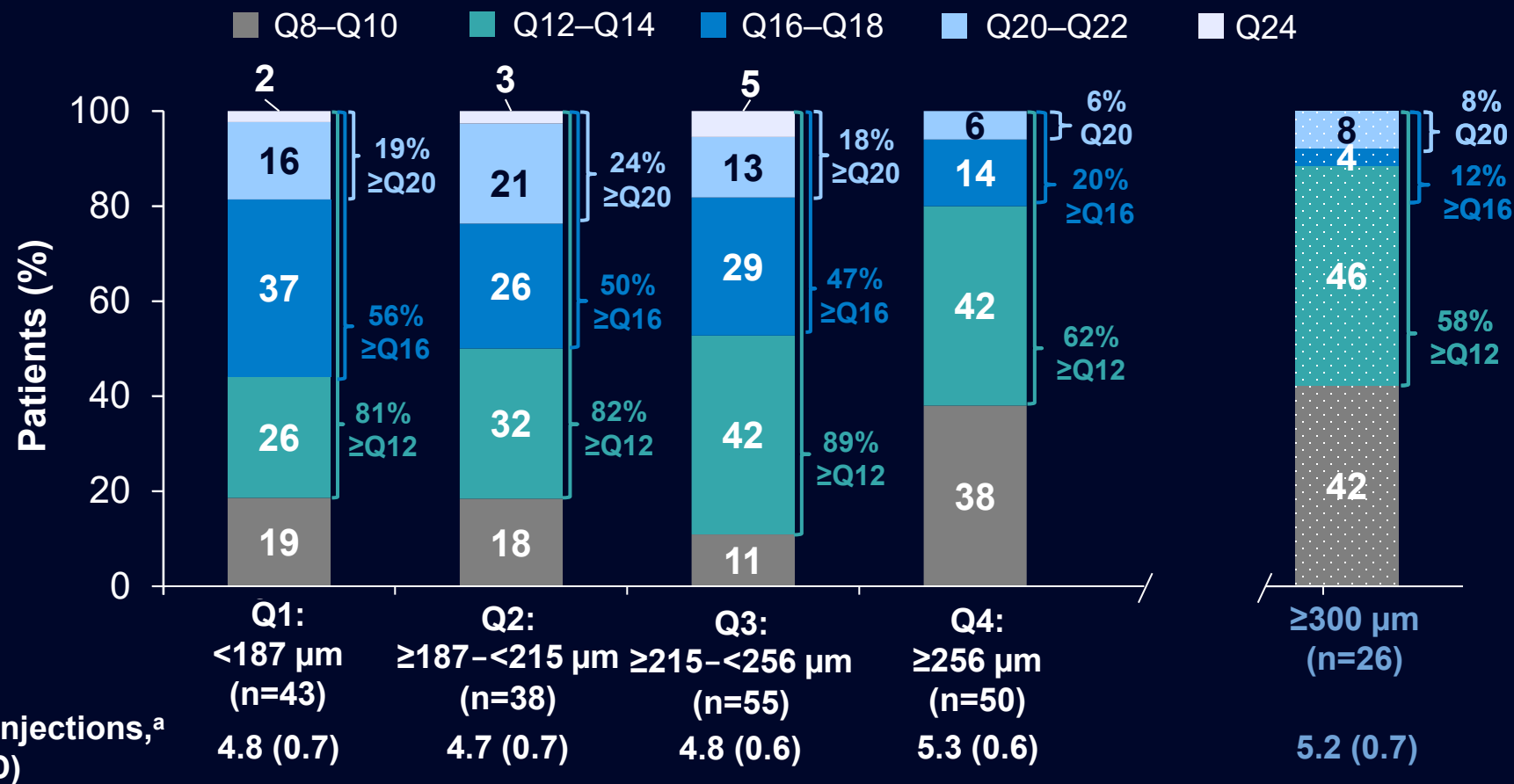


CRT, mean, μm^a	W96	W100	W156
Q1: $<187 \mu\text{m}$	157	157	151
Q2: $\geq 187 - <215 \mu\text{m}$	202	202	201
Q3: $\geq 215 - <256 \mu\text{m}$	230	221	232
Q4: $\geq 256 \mu\text{m}$	334	266	277
$\geq 300 \mu\text{m}$	389	295	301

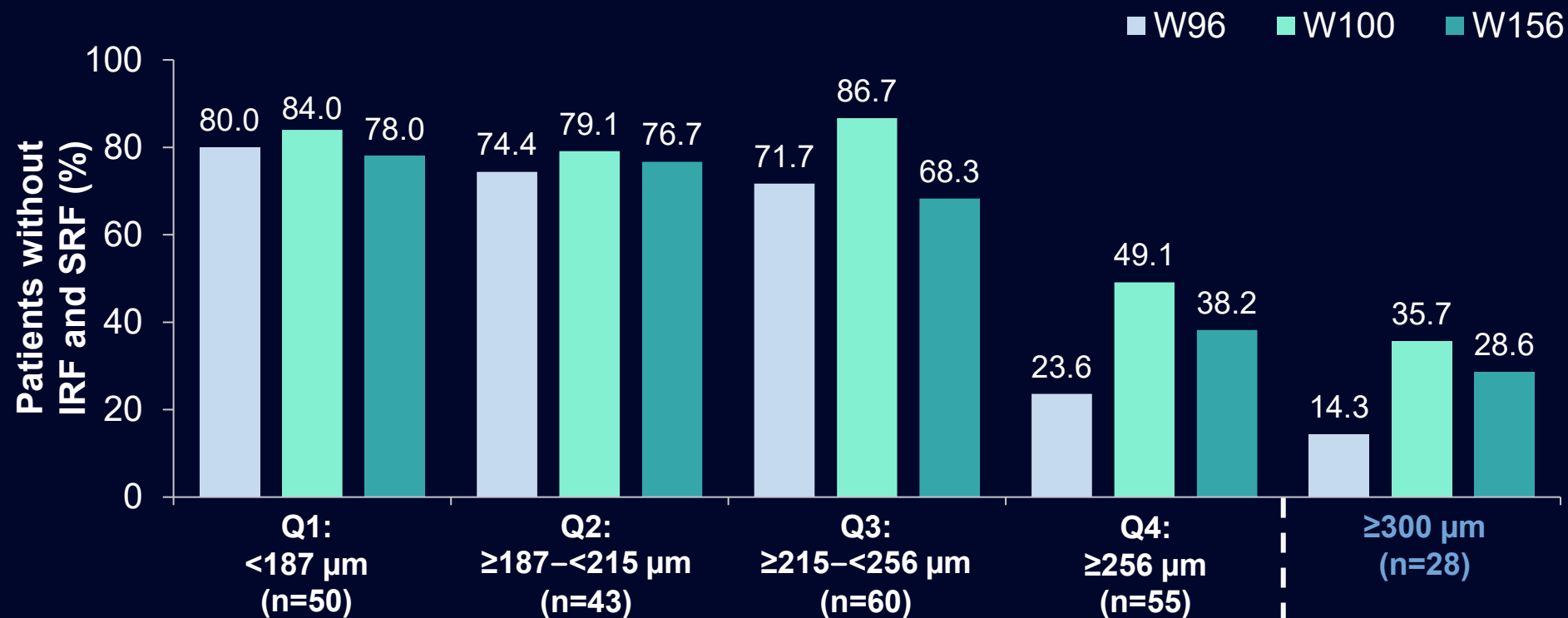
- Switching to aflibercept 8 mg resulted in more sustained CRT reductions over longer treatment intervals compared with 2 mg every 8 weeks
- In particular the Q4 and $\geq 300 \mu\text{m}$ groups demonstrated a further decrease in CRT following the switch to aflibercept 8 mg

Majority of Patients Were on $\geq$ Q12 Dosing Intervals Through W156 Irrespective of CRT Status At the Time of the Switch

Last assigned dosing intervals at W156 by W96 CRT quartiles and CRT $\geq 300 \mu\text{m}$



The Proportion of Patients Without IRF And SRF Was Maintained Or Increased At W156 After Switching To Aflibercept 8 mg



Conclusions

- BCVA gains achieved with aflibercept 2 mg were maintained through W156 after switching to aflibercept 8 mg at W96 across all W96 CRT quartiles and in patients with W96 CRT ≥ 300 μm , with lower number of injections
- Anatomic and fluid outcomes remained well-controlled, and most patients achieved ≥ 12 -week dosing intervals in the W96 CRT quartiles and CRT ≥ 300 μm subgroups
 - Patients in the W96 CRT quartile Q4 group and those with W96 CRT ≥ 300 μm showed the largest CRT reductions and improved fluid resolution
 - Switching to aflibercept 8 mg resulted in more sustained CRT reductions over longer treatment intervals compared with 2 mg every 8 weeks; in particular the Q4 and ≥ 300 μm groups demonstrated a further decrease in CRT following the switch to aflibercept 8 mg
- These data support aflibercept 8 mg as an efficacious option for patients with stable disease as well as those with persistent anatomic activity prior to switching