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Greater and more durable fluid resolution with aflibercept 8 mg versus aflibercept 2 mg in the PULSAR trial: A 96-week post hoc analysis

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Purpose

- This post hoc, exploratory analysis of the PULSAR Phase 3 trial evaluated fluid resolution (no intraretinal fluid [IRF] and no subretinal fluid [SRF]) in the central subfield with aflibercept 8 mg compared with aflibercept 2 mg 8 weeks after each matched number of active injections beginning from the third active injection in neovascular age-related macular degeneration (nAMD)

Conclusions

- **Greater fluid resolution and improvement in CRT** were observed with aflibercept 8 mg compared with aflibercept 2 mg **8 weeks after each matched number of active injections beginning from the third active injection**
- **Aflibercept 8 mg achieved durable fluid control** with extended dosing and fewer injections compared with aflibercept 2 mg through Week 96 in a substantial proportion **of patients with treatment-naïve nAMD**

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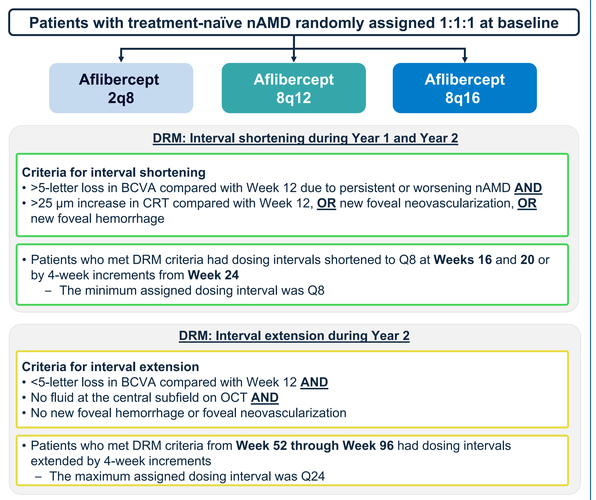
Methods

- In PULSAR (NCT04423718), patients were randomly assigned 1:1:1 to receive aflibercept 8 mg every 12 or 16 weeks (8q12 or 8q16) or aflibercept 2 mg every 8 weeks (2q8), each after 3 monthly injections. Dosing intervals for patients in the aflibercept 8q12 and 8q16 groups could be shortened from Week 16 and extended from Week 52 based on protocol criteria (**Figure 1**)
- Eligibility criteria included subfoveal choroidal neovascularization secondary to nAMD and the presence of IRF and/or SRF in the central subfield (defined as the circular area 1 mm in diameter centered on the fovea) of the study eye by optical coherence tomography at baseline

Figure 1: PULSAR study design



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; CRT, central retinal thickness; DRM, dose regiment modification; nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography.

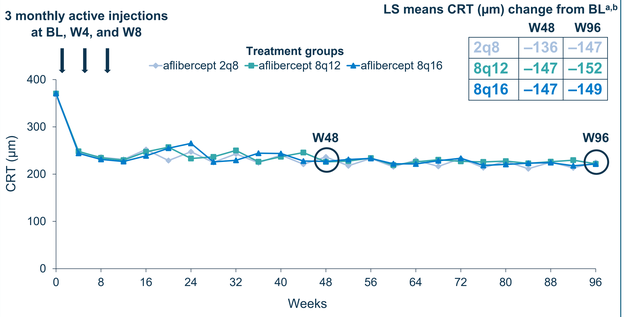
Results

- In the overall PULSAR population, central subfield retinal thickness (CRT) improved rapidly after the first injection for all 3 aflibercept groups, with comparable improvements through Week 48, which continued through Week 96 (**Figure 2**)
- As a key secondary endpoint, the proportion of patients with no IRF and no SRF in the central subfield 8 weeks after the third initial monthly injection at Week 16 was higher in the aflibercept 8 mg groups (8q12 and 8q16 groups) compared with the aflibercept 2 mg group (**Figure 3**)
- At Weeks 48 and 96, the proportion of patients without retinal fluid was comparable for patients receiving aflibercept 8 mg with extended dosing and fewer injections compared to patients receiving aflibercept 2 mg (**Figure 3**)
- Fluid control was sustained from Week 16 to Week 96 for IRF and SRF combined and IRF and SRF separately in all treatment groups (**Figure 3**)

Results

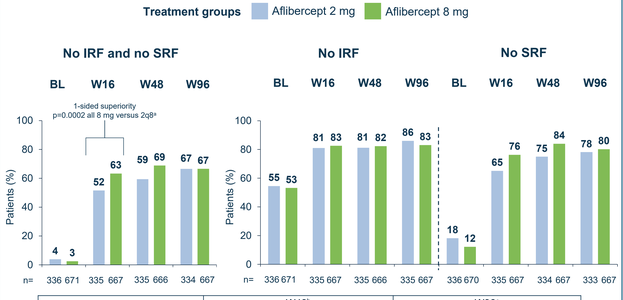
- In an exploratory post hoc analysis in patients with nAMD who received aflibercept 8 mg (8q12 or 8q16) or aflibercept 2 mg through Week 96, fluid was assessed 8 weeks after each matched number of active injections (beginning from the third active injection; **Figure 4**)
- The proportion of patients with fluid resolution was numerically higher in the aflibercept 8 mg groups than in the aflibercept 2 mg group, with a relative difference of 14–23%, beginning 8 weeks after the third active injection (**Figure 4**)
- At 8 weeks after active injections, there was a numerically higher change in CRT in patients in the aflibercept 8 mg groups than in the aflibercept 2 mg group, indicating more durable improvements in anatomic outcomes with aflibercept 8 mg (**Figure 5**)

Figure 2: Absolute CRT through Week 96



FAS: 2q8 n=336; 8q12 n=335; 8q16 n=338 (at BL). [a]LS mean values (data post-ICE were censored); [b]LS means were generated using MMRM, with baseline CRT measurement as a covariate, and treatment group (aflibercept 2q8, 8q12, 8q16), visit, and stratification variables (geographic region [Japan vs rest of world] and BL BCVA [<60 vs ≥60 letters]) as fixed factors, and interaction terms for baseline and visit and for treatment and visit. 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; FAS, full analysis set; ICE, intercurrent event; LS, least squares; MMRM, mixed model for repeated measures; W, week.

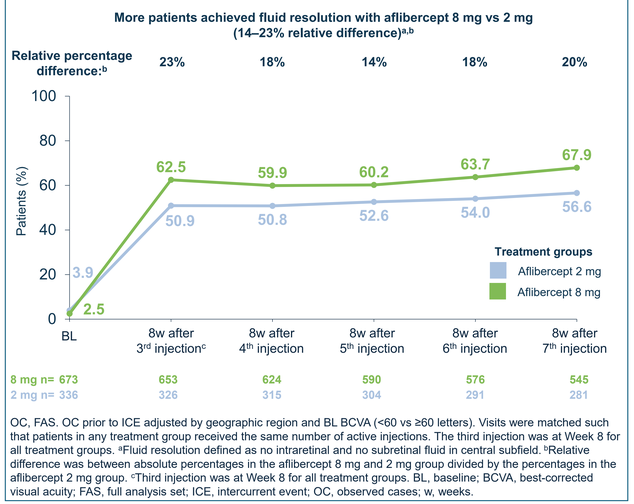
Figure 3: Proportion of patients with IRF and SRF resolution through Week 96



	W48[b]		W96[c]	
	2 mg	8 mg	2 mg	8 mg
Completers, n	309	628	286	583
Mean number of active injections	**6.9**	**5.6**	**12.8**	**9.0**

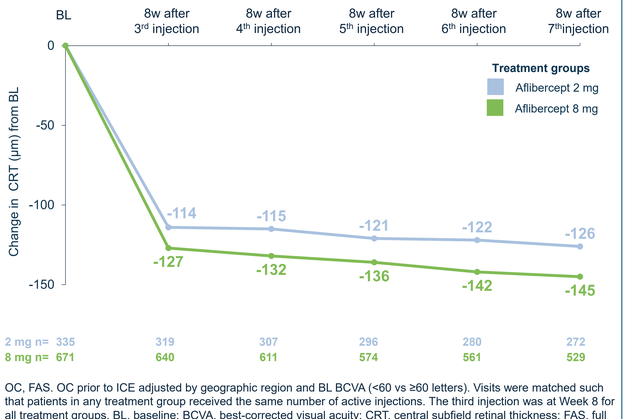
FAS, LOCF (censoring data post-ICE); FAS: 2q8 n=336; 8q12 n=335; 8q16 n=338; all 8 mg n=673.
[a]P-value: 1-sided CMH; weighting scheme adjusted by geographic region and BL BCVA (<60 vs ≥60 letters); [b]Patients completing Week 48; [c]Patients completing Week 96. BL, baseline; BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; FAS, full analysis set; ICE, intercurrent event; IRF, intraretinal fluid; LOCF, last observation carried forward; SRF, subretinal fluid; W, week.

Figure 4: Proportion of patients with fluid resolution 8 weeks after each matched number of active injections



OC, FAS. OC prior to ICE adjusted by geographic region and BL BCVA (<60 vs ≥60 letters). Visits were matched such that patients in any treatment group received the same number of active injections. The third injection was at Week 8 for all treatment groups. [a]Fluid resolution defined as no intraretinal and no subretinal fluid in central subfield. [b]Relative difference was between absolute percentages in the aflibercept 8 mg and 2 mg group divided by the percentages in the aflibercept 2 mg group. [c]Third injection was at Week 8 for all treatment groups. BL, baseline; BCVA, best-corrected visual acuity; FAS, full analysis set; ICE, intercurrent event; OC, observed cases; w, weeks.

Figure 5: CRT change from baseline 8 weeks after each matched number of active injections



OC, FAS. OC prior to ICE adjusted by geographic region and BL BCVA (<60 vs ≥60 letters). Visits were matched such that patients in any treatment group received the same number of active injections. The third injection was at Week 8 for all treatment groups. BL, baseline; BCVA, best-corrected visual acuity; CRT, central subfield retinal thickness; FAS, full analysis set; ICE, intercurrent event; OC, observed cases; w, weeks.

Disclosures

Richard Gale: Consultant for AbbVie, Allergan, Apellis, Bayer, Biogen, Boehringer Ingelheim, Notal, Novartis, Roche, and Santen; receives funding from Bayer, Novartis, and Roche.

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