Rapid fluid resolution with aflibercept 8 mg may be associated with extended dosing intervals at Week 96 in nAMD: A PULSAR post hoc analysis

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Disclosures

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- **Paolo Lanzetta:** Consultant for Aerie Pharmaceuticals, Allergan, Apellis, Bausch + Lomb, Bayer, Biogen, Boehringer Ingelheim, I-Care, Genentech, Novartis, Ocular Therapeutix, Outlook Therapeutics, and Roche
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PULSAR: 96-Week, Multicenter, Double-Masked Study in Patients With Treatment-Naïve nAMD

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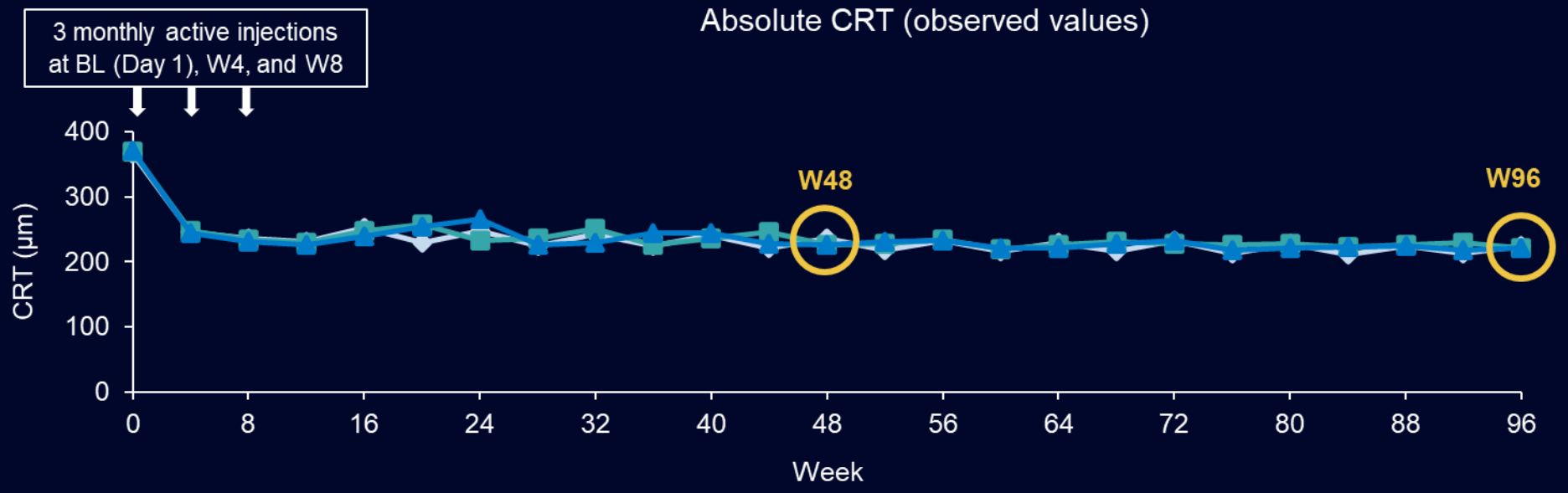
Patients were randomly assigned (1:1:1) to receive aflibercept 8q12 (n=335), 8q16 (n=338), or 2q8 (n=336), each after 3 monthly injections

- At W48, treatment with aflibercept 8 mg demonstrated non-inferior BCVA gains with extended dosing intervals versus aflibercept 2 mg in patients with nAMD,[1] with no new safety signals
- At W96, treatment with aflibercept 8 mg maintained improvements in visual and anatomic outcomes with extended dosing intervals, demonstrating long-term efficacy with no new safety signals



LS means CRT (µm) change from BL[a,b]

	W48	W96
2q8	–136	–147
8q12	–147	–152
8q16	–147	–149

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 MRMM, with BL 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]) as fixed factors, and interaction terms for BL and visit and for treatment 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; **nAMD**, neovascular age-related macular degeneration; **W**, week.

[1]Lanzetta P, et al. *Lancet*. 2024;403:1141–1152.

Analysis of Early Fluid Resolution and Its Association With the Last Assigned Dosing Interval at Week 96 in the Aflibercept 8 mg Group

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Objective:

To investigate whether early fluid resolution is associated with last assigned dosing interval at Week 96 in patients treated with aflibercept 8 mg

Methods:

The presence of fluid at Weeks 4, 8, and 12 (4 weeks after each injection) was analyzed in patients who completed 96 weeks of treatment. The association between fluid resolution at Weeks 4, 8, and 12 and the last assigned dosing interval at Week 96 in patients who received aflibercept 8 mg (8q12 and 8q16 groups) was analyzed, regardless of fluid outcomes at other timepoints

	Day 1	Week 4	Week 8	Week 12
Initial injections in both aflibercept 8 mg and 2 mg arms				
Patients who were fluid-free at Week 4		**Fluid-free**	/	/
Patients who were fluid-free at Weeks 4 and 8		**Fluid-free**	**Fluid-free**	/
Patients who were fluid-free at Weeks 4, 8, and 12		**Fluid-free**	**Fluid-free**	**Fluid-free**
Patients who were never fluid-free at Weeks 4, 8, and 12		**Fluid present**	**Fluid present**	**Fluid present**

Fluid status was not assessed on Day 1. Fluid status was defined as the absence (fluid-free) or presence (fluid present) of IRF and SRF in the central subfield. / = patients who were either fluid-free, not fluid-free, or with unknown fluid status. **IRF**, intraretinal fluid; **SRF**, subretinal fluid.

Last Assigned Dosing Interval at Week 96 of the Aflibercept 8 mg Groups Based on Early Fluid Status

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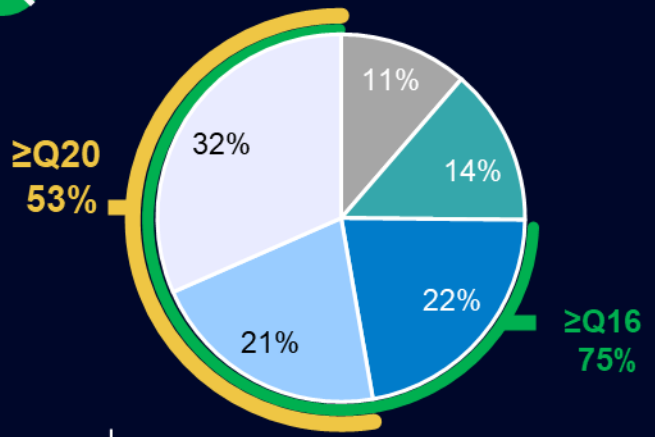
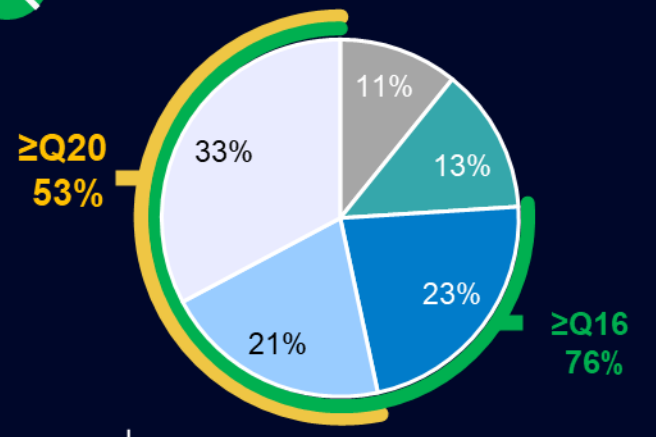
Last assigned dosing interval: Q8[a] Q12 Q16 Q20 Q24[b]

Fluid-free at Week 4 (56%; n=326)



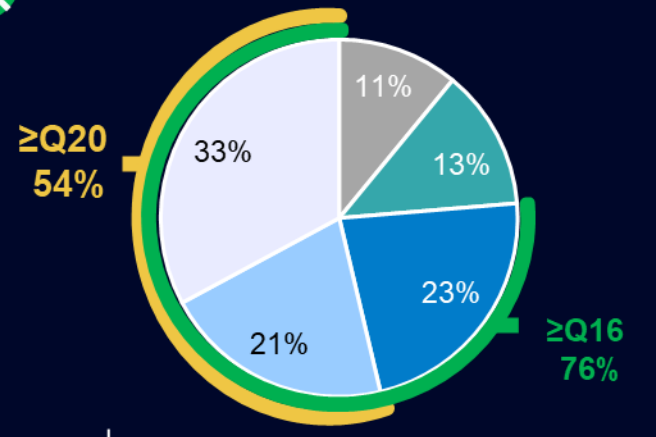
FAS, OC[c]	BCVA (ETDRS letters)	CRT (µm)
BL	61.1±12.2 (n=385)	339±110 (n=385)
Week 48	66.3±15.9 (n=330)	217±56 (n=325)
Week 96	65.9±17.4 (n=299)	213±58 (n=294)

Fluid-free at Weeks 4 and 8 (51%; n=296)



FAS, OC[c]	BCVA (ETDRS letters)	CRT (µm)
BL	61.6±12.0 (n=346)	334±105 (n=346)
Week 48	66.9±15.9 (n=298)	214±53 (n=294)
Week 96	66.3±17.7 (n=270)	213±56 (n=267)

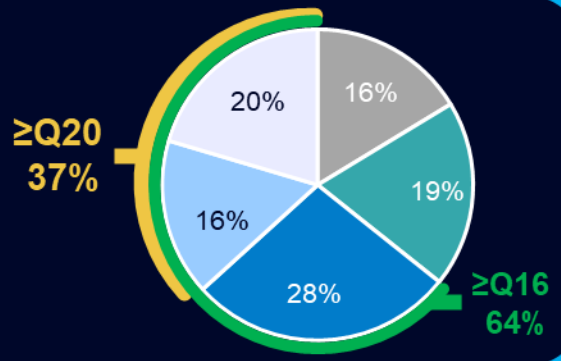
Fluid-free at Weeks 4, 8, and 12 (48.5%; n=283)



FAS, OC[c]	BCVA (ETDRS letters)	CRT (µm)
BL	61.8±11.9 (n=328)	333±105 (n=328)
Week 48	67.0±16.0 (n=285)	214±38 (n=326)
Week 96	66.3±17.9 (n=259)	213±56 (n=255)

Patients who were never fluid-free at Weeks 4, 8 and 12 (16.8%; n=98)

FAS, OC[c]	BCVA (ETDRS letters)	CRT (µm)
BL	56.0±14.4 (n=102)	439±159 (n=102)
Week 48	62.8±15.7 (n=94)	266±86 (n=87)
Week 96	62.8±16.9 (n=82)	247±83 (n=78)



- More patients who experienced rapid fluid resolution had a last assigned dosing interval of ≥16 or ≥20 weeks compared with those who were never fluid-free

FAS. Data shown for patients who completed 96 weeks of treatment. Values may not add up to 100% due to rounding. [a]Patients had their dosing interval shortened based on DRM assessments at some point through Week 96. [b]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period. [c]FAS. OC prior to ICE. **DRM**, dose modification regimen; **ETDRS**, Early Treatment Diabetic Retinopathy Study; **OC**, observed cases.

BCVA and CRT Outcomes in the Aflibercept 8 mg and 2 mg Groups Through Week 96 Based on Early Fluid Resolution

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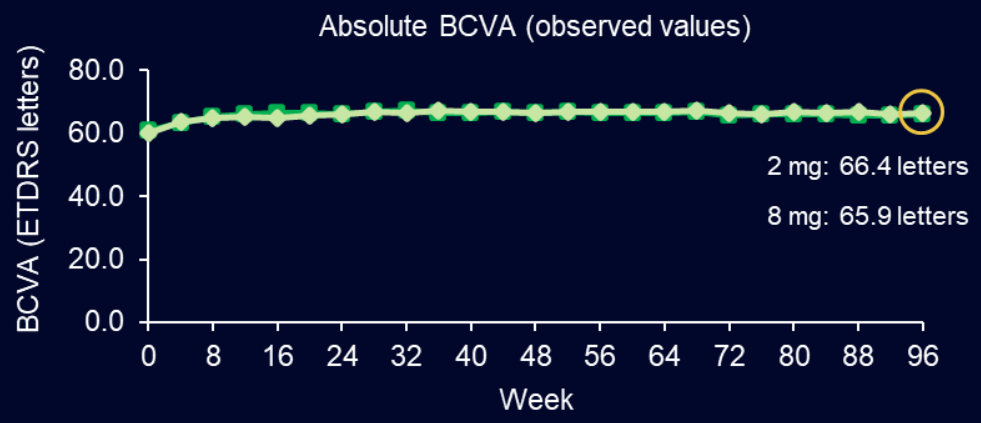
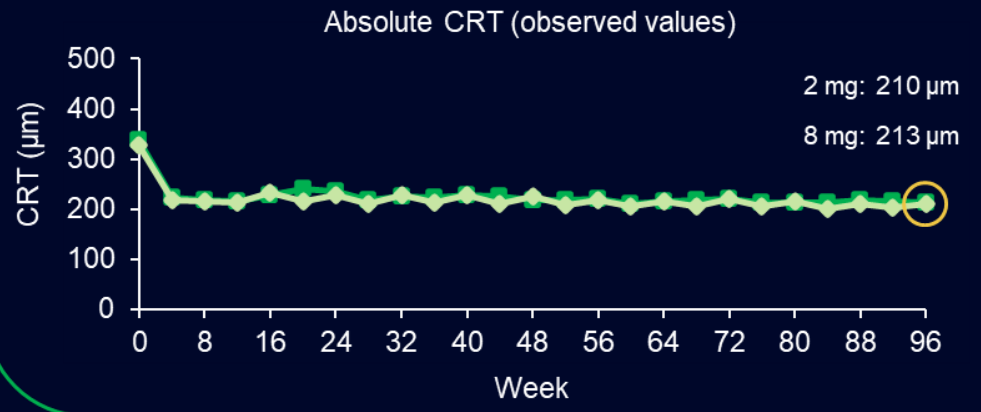
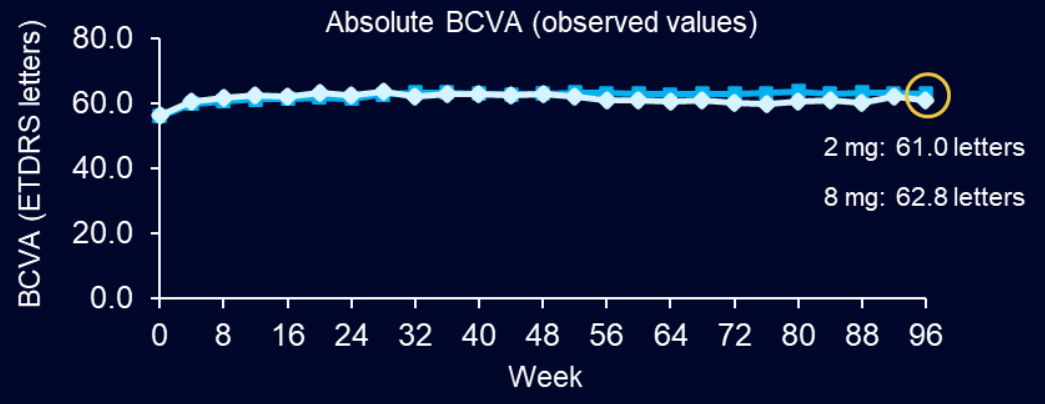
Treatment groups 2 mg group 8 mg group

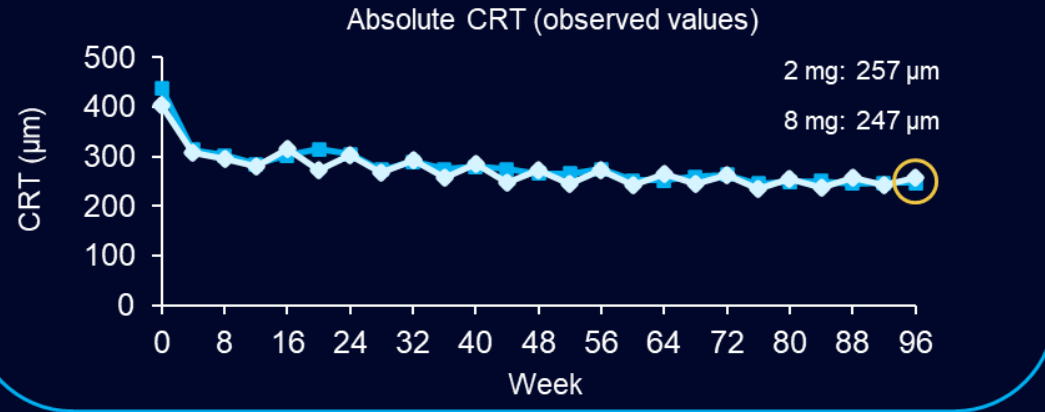
Patients who were fluid-free at Week 4





Patients who were never fluid-free at Weeks 4, 8, and 12





- Rapid BCVA gains and CRT reductions were observed after the first injection and were sustained over 96 weeks

FAS (OC prior to ICE).

Conclusion

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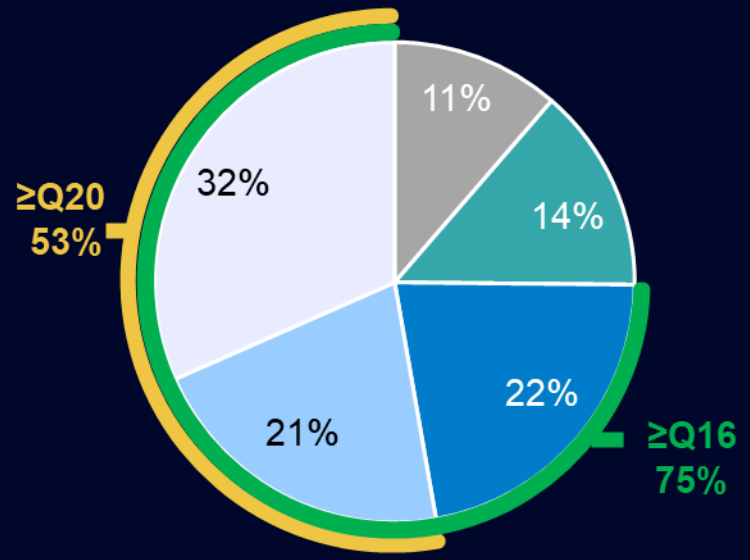
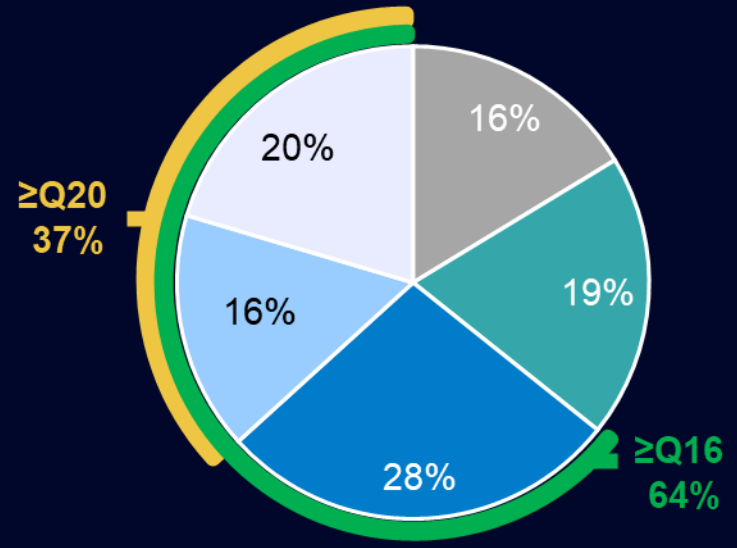
Last assigned dosing interval: Q8[a] Q12 Q16 Q20 Q24[b]

Fluid-free at Week 4



Patients who were never fluid-free at Weeks 4, 8 and, 12



- Rapid fluid resolution during the initial monthly treatment phase may be associated with extended dosing intervals in patients who received aflibercept 8 mg for nAMD

FAS. Data shown for patients who completed 96 weeks of treatment. Values may not add up to 100% due to rounding. [a]Patients shortened based on DRM assessments at some point through Week 96. [b]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.