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Clinical outcomes with aflibercept 8 mg and aflibercept 2 mg are generally comparable in patients grouped by CNV type: A post hoc analysis of the 96-week PULSAR trial

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Purpose

- A post hoc analysis was conducted to evaluate clinical outcomes with aflibercept 8 mg and aflibercept 2 mg in the PULSAR trial in patients with neovascular age-related macular degeneration (nAMD) grouped by baseline (BL) choroidal neovascularization (CNV) type

Conclusions

- In **PULSAR, improvements in BCVA and CRT** were observed from baseline at Week 96 with **both aflibercept 8 mg and 2 mg** in **patients grouped by baseline CNV type**
  - **Generalizability** of the findings may be **limited** by the post hoc nature of this analysis; **smaller subgroup size** may result in **larger variability**
- The **safety profile** of **aflibercept 8 mg was consistent with that of 2 mg** across the overall PULSAR population

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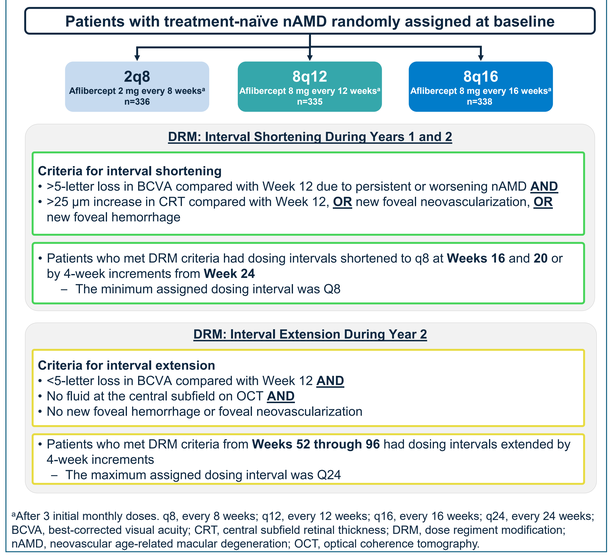
Methods

- In the 96-week Phase 3 trial, PULSAR (NCT04423718), treatment-naïve patients with nAMD were randomly assigned 1:1:1 to receive intravitreal aflibercept 8 mg every 12 (8q12) or 16 weeks (8q16), or 2 mg every 8 weeks (2q8), each after 3 initial monthly injections (**Figure 1**)
- From Week16, dosing intervals in the 8q12 and 8q16 arms were modified if predefined criteria were met
- In this post hoc analysis, clinical outcomes through Week 96 were evaluated by BL CNV type, as assessed by fundus photography, fluorescein angiography, and optical coherence tomography by masked readers at a central reading center

Figure 1: PULSAR study design



[a]After 3 initial monthly doses. q8, every 8 weeks; q12, every 12 weeks; q16, every 16 weeks; q24, every 24 weeks; BCVA, best-corrected visual acuity; CRT, central subfield retinal thickness; DRM, dose regiment modification; nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography.

Results

- At BL, 59.1% (n=596) of patients in the PULSAR trial presented with CNV Type 1, 19.3% (n=195) with Type 2, 20.0% (n=202) with Mixed (Type 1 and Type 2), and 1.4% (n=14) with Type 3
  - Patients with Type 3 CNV were not evaluated here due to the small subgroup size
- Within the Type 1, Type 2, and Mixed CNV type subgroups, the patients' demographics and disease characteristics at BL were generally comparable across the 3 treatment arms (**Table 1**)
- Improvements in BCVA from BL at Week 96 were observed across the 2q8, 8q12, and 8q16 treatment arms in patients stratified by BL CNV type (**Figure 2**)
- Clinically relevant improvements in CRT from BL at Week 96 were observed, with no marked differences across the 3 treatment arms within each subgroup (**Figure 3**)

Results

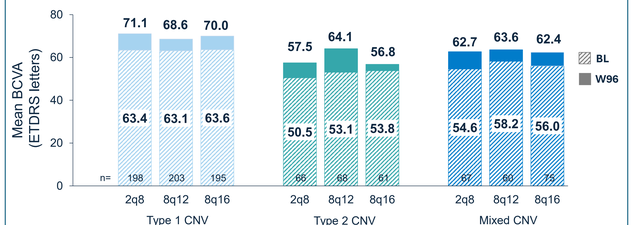
- Across each CNV subtype group, most patients in the 8q12 and 8q16 arms had a last assigned dosing interval with aflibercept 8 mg of ≥12 or ≥16 weeks, respectively, at Week 96 (**Figure 4**)
- The safety profile of aflibercept 8 mg was consistent with that of 2 mg in the overall PULSAR population (**Table 2**); the most common ocular TEAEs overall were cataract, reduced visual acuity, and retinal hemorrhage

Table 1: Baseline demographics and disease characteristics of the CNV type subgroups

		2q8	8q12	8q16
Type 1 CNV n=596 (59.1%)	n	198	203	195
	Female, %	58.1	57.6	54.4
	BCVA, ETDRS letters	63.4 (11.9)	63.1 (12.4)	63.6 (11.4)
	CRT, µm	327 (108)	338 (107)	338 (119)
	CNV size, mm²	7.1 (5.3)	6.3 (4.5)	7.0 (5.5)
Type 2 CNV n=195 (19.3%)	n	65	68	61
	Female, %	50.0	50.0	50.8
	BCVA, ETDRS letters	50.5 (15.0)	53.1 (12.8)	53.8 (12.6)
	CRT, µm	442 (148)	429 (140)	419 (155)
	CNV size, mm²	3.6 (3.1)	3.2 (3.6)	3.1 (3.9)
Mixed CNV[a] n=202 (20.0%)	n	67	60	75
	Female, %	53.7	46.7	52.0
	BCVA, ETDRS letters	54.6 (13.7)	58.2 (12.6)	56.0 (11.7)
	CRT, µm	406 (141)	398 (114)	416 (126)
	CNV size, mm²	6.9 (4.9)	8.0 (5.7)	8.2 (5.6)

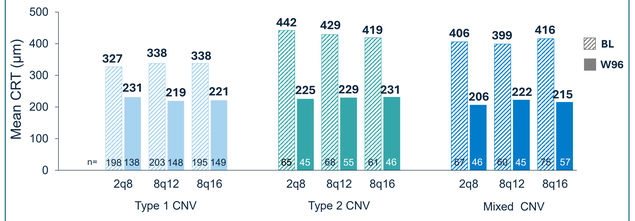
FAS. Data are mean (SD) unless otherwise indicated. [a]Mixed CNV type consists of Type 1 and Type 2 CNV types. Type 3 CNVs were observed in 1.4% of cases (n=14), with 5, 4, and 5 cases in the 2q8, 8q12, and 8q16 arms, respectively. ETDRS, Early Treatment Diabetic Retinopathy Study; FAS, full analysis set; SD, standard deviation.

Figure 2: Mean BCVA at baseline and Week 96 for each CNV subtype



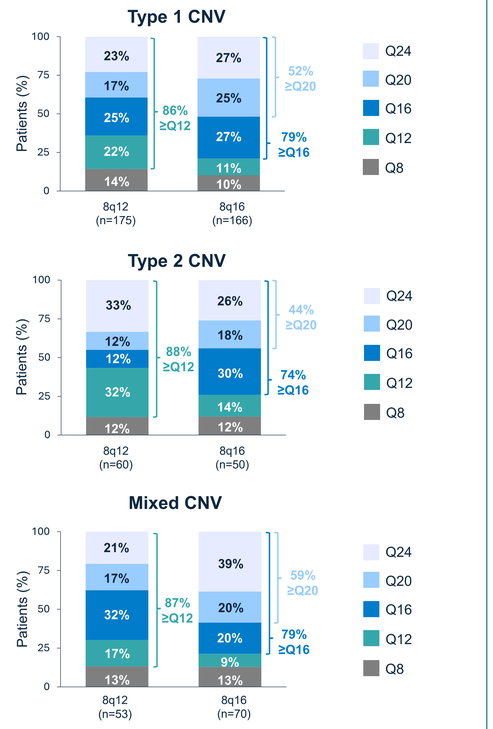
FAS (observed cases prior to intercurrent events); n values represent the number of patients at BL. LS mean changes[a] from BL at Week 96 in the 2q8, 8q12, and 8q16 arms were 6.6, 4.0, and 5.8 letters for Type 1, 6.5, 10.3, and 3.6 letters for Type 2, and 7.3, 5.7, and 6.7 letters for Mixed, respectively. [a]LS means were generated using MMRM, with BL BVCA 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 BL and visit and for treatment and visit. LS, least squares; MMRM, mixed model repeated measures.

Figure 3: Mean CRT at baseline and Week 96 for each CNV subtype



FAS (observed cases prior to intercurrent events). LS mean changes[a] from BL at Week 96 in the 2q8, 8q12, and 8q16, and arms were −104, −116, and −116 µm for Type 1, −201, −202, and −194 µm for Type 2, and −196, −181, −181 µm for Mixed, respectively. [a]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 letters]) as fixed factors, and interaction terms for BL and visit and for treatment and visit.

Figure 4: Last assigned dosing interval at Week 96



FAS, patients completing Week 96. Values may not add up to 100% due to rounding.

Table 2: Safety through Week 96 in the overall PULSAR population

	2q8 n=336	All 8 mg n=673
Any ocular TEAEs, n (%)	181 (53.9)	345 (51.3)
Any non-ocular TEAEs, n (%)	257 (76.5)	500 (74.3)

SAF. TEAEs were adverse events that occurred from the first injection to 30 days after the last injection (active or sham); ocular TEAEs were those that occurred in the study eye. SAF, safety analysis set; TEAE, treatment-emergent adverse event.

Disclosures

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