Pooled Safety Analysis of Aflibercept 8 mg in the CANDELA, PULSAR, PHOTON, and QUASAR Trials

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Anita Barikian, MD, on behalf of the CANDELA, PULSAR, PHOTON, and QUASAR study investigators
Retina Care Specialists, Palm Beach Gardens, Florida

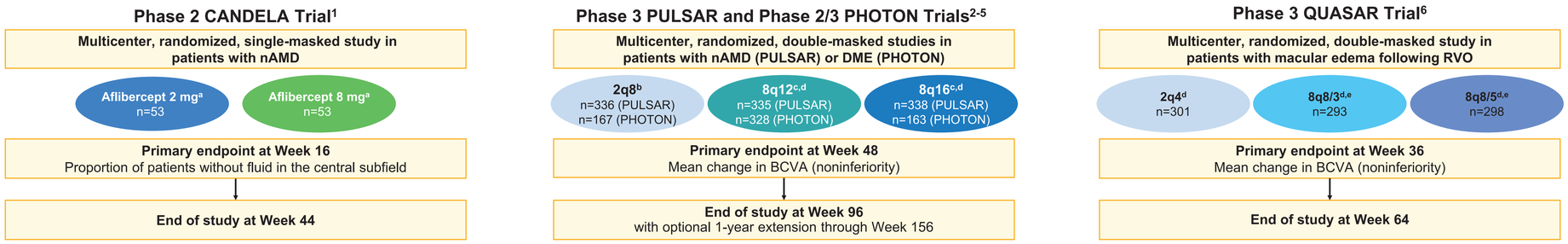
BACKGROUND & PURPOSE

- Aflibercept 8 mg first demonstrated similar efficacy and safety to aflibercept 2 mg in the phase 2 CANDELA trial in patients with neovascular age-related macular degeneration (nAMD)[1]
- In subsequent pivotal trials, aflibercept 8 mg at extended dosing intervals had comparable efficacy and safety to aflibercept 2 mg in the patients with nAMD (PULSAR), diabetic macular edema (PHOTON), and macular edema following retinal vein occlusion (RVO)[2-6]
- In each of these trials, the ocular and systemic safety profile of aflibercept 8 mg was shown to be consistent with that for aflibercept 2 mg
- An evaluation of safety data from multiple trials can provide a comprehensive understanding of the safety profile of aflibercept 8 mg across several retinal diseases
- A pooled analysis evaluating the safety of aflibercept 8 mg and 2 mg up to 96 weeks was conducted using available data across the CANDELA, PULSAR, PHOTON, and QUASAR trials

METHODS

- Data for the safety analysis set from 4 multicenter, randomized clinical trials (**Figure 1**) comparing the efficacy and safety of aflibercept 8 mg versus aflibercept 2 mg were pooled
- Treatment-emergent adverse events (TEAEs) reported by study investigators were coded using the latest available version of Medical Dictionary for Regulatory Activities (MedDRA®)
- Reported terms were pooled for the purpose of this analysis, and data were summarized descriptively

Figure 1. Study Designs of Clinical Trials Evaluating Aflibercept 8 mg in Patients With nAMD, DME, and macular edema following RVO



[a]Three initial monthly injections followed by injections at Weeks 20 and 32. [b]After 3 (PULSAR) or 5 (PHOTON) initial monthly injections. [c]After 3 initial monthly injections. [d]With opportunity for extension per dose-regimen modification. [e]After 3 (8q8/3) or 5 (8q8/5) initial monthly injections.
2q4, aflibercept 2 mg every 4 weeks; 2q8, aflibercept 2 mg every 8 weeks; 8q8/3, aflibercept 8 mg every 8 weeks after 3 initial monthly injections; 8q8/5, aflibercept 8 mg every 8 weeks after 5 initial monthly injections; 8q12, aflibercept 8 mg every 12 weeks; 8q16, aflibercept 8 mg every 16 weeks; BCVA, best-corrected visual acuity.

RESULTS

- Overall, safety data for 2665 patients, of which 1808 received aflibercept 8 mg and 857 received aflibercept 2 mg, were evaluated (**Table 1**)

Table 1. Patients Evaluated in the Pooled Safety Analysis

	Aflibercept 2 mg pooled (n=857)	Aflibercept 8 mg pooled[a] (n=1808)
CANDELA, n	53	53
PULSAR, n	336	673
PHOTON, n	167	491
QUASAR, n	301	591
Total, n	857	1808

[a]All aflibercept 8 mg treatment groups from each trial were pooled.

- Baseline demographics of patients in the pooled aflibercept 8 mg and 2 mg groups were generally similar (**Table 2**)
- The mean number of injections for the pooled aflibercept 8 mg and 2 mg groups was 8.4 and 11.5, respectively (**Table 2**)

Table 2. Baseline Demographics and Aflibercept Exposure

	Aflibercept 2 mg pooled (n=857)	Aflibercept 8 mg pooled (n=1808)
Female, n (%)	443 (51.7)	856 (47.3)
Age group, n (%)		
<65 years	266 (31.0)	602 (33.3)
≥65-<75 years	299 (34.9)	629 (34.8)
≥75 years	292 (34.1)	577 (31.9)
White, n (%)	590 (68.8)	1277 (70.6)
Hispanic or Latino, n (%)	69 (8.1)	143 (7.9)
Total number of injections	9836	15,090
Number of injections, mean (SD)	11.5 (2.9)	8.4 (2.0)
Treatment duration, mean (SD), weeks	75.9 (23.7)	78.1 (23.4)

SD, standard deviation.

- The incidence of ocular TEAEs was comparably low between the pooled aflibercept 8 mg and 2 mg groups (**Table 3**)
  - The most common ocular TEAE was cataract, which was reported in 9.3% and 8.2% of patients in the pooled aflibercept 8 mg and 2 mg groups, respectively
- No cases of occlusive retinal vasculitis were reported through Week 96

Table 3. Ocular and Serious Ocular TEAEs in the Study Eye

	Aflibercept 2 mg pooled (n=857)	Aflibercept 8 mg pooled (n=1808)
Patients with ≥1 ocular TEAE, n (%)	390 (45.5)	835 (46.2)
Ocular TEAEs occurring in ≥3% of patients in any group, n (%)		
Cataract[a]	70 (8.2)	168 (9.3)
Visual acuity reduced	42 (4.9)	78 (4.3)
Conjunctival hemorrhage	25 (2.9)	72 (4.0)
IOP increased	25 (2.9)	69 (3.8)
Vitreous detachment	20 (2.3)	64 (3.5)
Vitreous floaters	26 (3.0)	58 (3.2)
Patients with ≥1 serious ocular TEAE, n (%)	15 (1.8)	38 (2.1)
Serious ocular TEAEs in ≥2 patients in any group, n (%)		
Cataract[b]	1 (0.1)	8 (0.4)
Retinal detachment	2 (0.2)	6 (0.3)
Retinal hemorrhage	1 (0.1)	4 (0.2)
IOP increased	0	3 (0.2)
Vitreous hemorrhage	0	3 (0.2)
Retinal tear	0	2 (0.1)
Skin laceration	0	2 (0.1)
Endophthalmitis	4 (0.5)	1 (<0.1)
Visual acuity reduced	2 (0.2)	1 (<0.1)
Macular hole	2 (0.2)	0

[a]Includes cataract, cataract cortical, cataract nuclear, cataract operation, cataract subcapsular, lenticular opacities, and posterior capsule opacification, although not all terms met the ≥3% threshold. [b]Includes cataract, cataract nuclear, and cataract subcapsular, although not all terms met the ≥2 patient threshold.
IOP, intraocular pressure.

- The incidence of intraocular inflammation (IOI) was low and comparable between the pooled aflibercept 8 mg and 2 mg groups (**Table 4**)
  - Most cases were non-serious and mild or moderate in severity

Table 4. IOI in the Study Eye

	Aflibercept 2 mg pooled (n=857)	Aflibercept 8 mg pooled (n=1808)
IOI, n (%)	14 (1.6)	22 (1.2)
Uveitis	2 (0.2)	4 (0.2)
Iritis	0	4 (0.2)
Vitritis	0	4 (0.2)
Iridocyclitis	2 (0.2)	4 (0.2)
Vitreal cells	2 (0.2)	2 (0.1)
Anterior chamber cell	2 (0.2)	2 (0.1)
Endophthalmitis	5 (0.6)	1 (<0.1)
Chorioretinitis	0	1 (<0.1)
Eye inflammation	2 (0.2)	0
Hypopyon	1 (0.1)	0

- The incidence of IOP- and glaucoma-related TEAEs was low and comparable between the pooled aflibercept 8 mg and 2 mg groups (**Tables 5** and **6**)
  - Paracentesis rates were low, occurring in 0.7% and 0.2% of patients in the pooled aflibercept 8 mg and 2 mg groups, respectively

Table 5. IOP in the Study Eye

	CANDELA		PULSAR		PHOTON		QUASAR	
	Aflibercept 2 mg (n=53)	Aflibercept 8 mg (n=53)	Aflibercept 2 mg (n=336)	Aflibercept 8 mg (n=673)[a]	Aflibercept 2 mg (n=167)	Aflibercept 8 mg (n=491)[a]	Aflibercept 2 mg (n=301)	Aflibercept 8 mg (n=591)[b]
IOP increase from baseline ≥10mmHg pre-dose at any visit, n (%)	0	2 (3.8)	11 (3.3)	18 (2.7)	5 (3.0)	28 (5.7)	8 (2.7)	32 (5.4)
IOP ≥35 mmHg pre- or post-dose at any visit, n (%)	0	0	2 (0.6)	4 (0.6)	2 (1.2)	2 (0.4)	2 (0.7)	7 (1.2)

[a]Data for the aflibercept 8q12 and 8q16 groups were pooled. [b]Data for the aflibercept 8q8/3 and 8q8/5 groups were pooled.

Table 6. Rates of IOP- and Glaucoma-Related TEAEs, and Paracentesis in the Study Eye

	Aflibercept 2 mg pooled (n=857)	Aflibercept 8 mg pooled (n=1808)
IOP- and glaucoma-related TEAEs, n (%)	37 (4.3)	102 (5.6)
IOP increased	25 (2.9)	69 (3.8)
Ocular hypertension	8 (0.9)	20 (1.1)
Glaucoma	2 (0.2)	13 (0.7)
Borderline glaucoma	0	5 (0.3)
Open-angle glaucoma	1 (0.1)	3 (0.2)
Angle closure glaucoma	2 (0.2)	2 (0.1)
Glaucomatous optic neuropathy	1 (0.1)	0
Paracentesis procedures, n (%)	2 (0.2)	12 (0.7)

- The incidence of non-ocular TEAEs was comparable between the pooled aflibercept 8 mg and 2 mg groups (**Table 7**)
- The incidence of Antiplatelet Trialists' Collaboration (APTC) events and treatment-emergent deaths was comparable between the pooled aflibercept 8 mg and 2 mg groups (**Table 7**)

Table 7. Non-Ocular TEAEs, APTC Events, and Deaths

	Aflibercept 2 mg pooled (n=857)	Aflibercept 8 mg pooled (n=1808)
Patients with ≥1 non-ocular TEAE, n (%)	585 (68.3)	1252 (69.2)
Non-ocular TEAEs occurring in ≥5% of patients in any group, n (%)		
COVID-19	86 (10.0)	232 (12.8)
Hypertension	56 (6.5)	170 (9.4)
Nasopharyngitis	59 (6.9)	127 (7.0)
Urinary tract infection	44 (5.1)	68 (3.8)
Patients with ≥1 serious non-ocular TEAE, n (%)	148 (17.3)	322 (17.8)
Patients with ≥1 APTC event,[a] n (%)	29 (3.4)	54 (3.0)
Non-fatal myocardial infarction	11 (1.3)	21 (1.2)
Vascular death	11 (1.3)	17 (0.9)
Non-fatal stroke	7 (0.8)	16 (0.9)
Treatment-emergent deaths, n (%)	20 (2.3)	38 (2.1)

[a]Events adjudicated as arterial thromboembolic events according to the APTC criteria.

CONCLUSIONS

- In this pooled safety analysis of data for 2665 patients with nAMD, DME, or RVO across 4 clinical trials, the safety profile for aflibercept 8 mg was comparable to that for aflibercept 2 mg up to 96 weeks
- The incidence of IOI was low and comparable between the pooled aflibercept 8 mg and 2 mg groups
  - One case of endophthalmitis was reported in the pooled aflibercept 8 mg group, whereas 5 cases of endophthalmitis were reported in the pooled aflibercept 2 mg group
- The incidence of IOP- and glaucoma-related TEAEs and paracentesis procedures was low and comparable between the pooled aflibercept 8 mg and 2 mg groups
- The incidence of non-ocular TEAEs, including serious non-ocular TEAEs, APTC events, and treatment-emergent deaths, was similar between the pooled aflibercept 8 mg and 2 mg groups

REFERENCES

1. Wykoff CC et al. *JAMA Ophthalomology.* 2023;141(9):834–842.
2. Brown DM et al. *Lancet.* 2024;403:1153–1163.
3. Do DV et al. *Ophthalmology.* 2025;S0161-6420(25)00707–9.
4. Lanzetta P et al. *Lancet.* 2024;403:1141–1152.
5. Korobelnik J-F et al. *Ophthalmology*. 2026;133:39–50.
6. Chaudhary V. Presented at: Angiogenesis , Exudation, and Degeneration Virtual Meeting; February 7, 2026.

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