Safety Profile of Aflibercept 8 mg: A Pooled Analysis of the CANDELA, PULSAR, PHOTON, and QUASAR Trials

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Disclosures

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Background

- Aflibercept 8 mg has demonstrated comparable efficacy and safety to aflibercept 2 mg in the pivotal PULSAR trial in nAMD, PHOTON trial in DME, and the QUASAR trial in MEfRVO[1–5]
- 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

This analysis evaluated the pooled safety of aflibercept 8 mg and 2 mg for up to 96 weeks across the CANDELA, PULSAR, PHOTON, and QUASAR trials

DME, diabetic macular edema; MEfRVO, macular edema following retinal vein occlusion; nAMD, neovascular age-related macular degeneration.

1. Brown DM et al. *Lancet.* 2024;403:1153–1163. 2. Do DV et al. *Ophthalmology.* 2025;S0161-6420(25)00707–9. 3. Lanzetta P et al. *Lancet.* 2024;403:1141–1152. 4. Korobelnik J-F et al. *Ophthalmology*. 2026;133:39–50. 5. Gale R. Presented at: FLORetina ICOOR Meeting; December 6, 2025; Florence, Italy.

Methods

- Data from 4 multicenter, randomized clinical trials comparing the efficacy and safety of aflibercept 8 mg versus aflibercept 2 mg were pooled:
  - 44-week, Phase 2 **CANDELA trial** in treatment-naïve patients with nAMD
  - 96-week, Phase 3 **PULSAR trial** in treatment-naïve patients with nAMD
  - 96-week, Phase 2/3 **PHOTON trial** in treatment-naïve and previously treated patients with DME
  - 64-week, Phase 3 **QUASAR trial** in treatment-naïve patients with MEfRVO

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

- TEAEs reported by investigators were coded using the latest available version of MedDRA®
- Reported terms were pooled for the purpose of this analysis, and data were summarized descriptively

[a]All aflibercept 8 mg treatment groups from each trial were pooled.
MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event.

Baseline Demographics and Aflibercept Exposure

	Aflibercept 2 mg pooled (n=857)	Aflibercept 8 mg pooled (n=1808)
Baseline demographics		
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)
Aflibercept exposure		
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)

Safety analysis set.
SD, standard deviation.

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)

No cases of occlusive retinal vasculitis were reported in the pooled aflibercept 8 mg or 2 mg groups

Safety analysis set.
[a]Includes cataract, cataract cortical, cataract nuclear, cataract operation, cataract subcapsular, lenticular opacities, and posterior capsule opacifications, although not all terms met the ≥3% threshold.
IOP, intraocular pressure.

Serious Ocular TEAEs in the Study Eye

	Aflibercept 2 mg pooled (n=857)	Aflibercept 8 mg pooled (n=1808)
Patients with ≥1 serious ocular TEAE, n (%)	**15 (1.8)**	**38 (2.1)**
Serious ocular TEAEs in ≥2 patients in any group, n (%)		
Cataract[a]	1 (0.1)	8 (0.4)
Retinal detachment	2 (0.2)	6 (0.3)
Retinal hemorrhage	1 (0.1)	4 (0.2)
Vitreous hemorrhage	0	3 (0.2)
IOP increased	0	3 (0.2)
Retinal tear	0	2 (0.1)
Skin laceration	0	2 (0.1)
Visual acuity reduced	2 (0.2)	1 (<0.1)
Endophthalmitis	4 (0.5)	1 (<0.1)
Macular hole	2 (0.2)	0

The incidence of serious ocular TEAEs was comparably low in the pooled aflibercept 8 mg and 2 mg groups

Safety analysis set.
[a]Includes cataract, cataract nuclear, and cataract subcapsular, although not all terms met the ≥2 patient threshold.

IOI-Related TEAEs in the Study Eye

	Aflibercept 2 mg pooled (n=857)	Aflibercept 8 mg pooled (n=1808)
IOI-related TEAEs, 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 IOI-related events was low and comparable in the pooled aflibercept 8 mg and 2 mg groups

Most IOI cases were non-serious and mild or moderate in severity

Safety analysis set.
IOI, intraocular inflammation.

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 ≥10 mmHg 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.
8q8/3, aflibercept 8 mg administered every 8 weeks after 3 initial monthly doses; 8q8/5, aflibercept 8 mg administered every 8 weeks after 5 initial monthly doses; 8q12, aflibercept 8 mg administered every 12 weeks, or every 12 weeks with pro re nata dosing after initial monthly doses; 8q16, aflibercept 8 mg administered every 16 weeks after initial monthly doses.

IOP- and Glaucoma-Related TEAEs 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

The incidence of IOP- and glaucoma-related TEAEs was low and comparable in both groups

The rate of paracentesis procedures was low, with 0.7% of patients in the pooled aflibercept 8 mg group and 0.2% of patients in the pooled aflibercept 2 mg group requiring paracentesis

Safety analysis set.

Non-ocular TEAEs

	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)

The incidence of non-ocular TEAEs was comparable in the pooled aflibercept 8 mg and 2 mg groups

Safety analysis set.

Potentially Clinically Significant Blood Pressure Values

	CANDELA		PULSAR		PHOTON		QUASAR	
	Aflibercept 2 mg (n=53)	Aflibercept 8 mg (n=53)	Aflibercept 2 mg (n=335)[a]	Aflibercept 8 mg (n=671)[a,b]	Aflibercept 2 mg (n=165)[c]	Aflibercept 8 mg (n=489)[b,c]	Aflibercept 2 mg (n=301)[d]	Aflibercept 8 mg (n=591)[d,e]
Systolic BP ≥160 mmHg and increase from baseline ≥20 mmHg, n (%)	9 (17.0)	6 (11.3)	41 (12.2)	87 (13.0)	51 (30.9)	154 (31.5)	27[f] (9.0)	52[g] (8.9)
Diastolic BP ≥110 mmHg and increase from baseline ≥10 mmHg, n (%)	1 (1.9)	0	4 (1.2)	3 (0.4)	4 (2.4)	18 (3.7)	2[f] (0.7)	14[g] (2.4)

[a]Patients at baseline without an abnormal BP assessment and ≥1 valid BP value after treatment initiation. Patients with missing or abnormal values at baseline were excluded.
[b]Data for the aflibercept 8q12 and 8q16 groups were pooled.
[c]Patients with a valid post-baseline BP value.
[d]Patients without an abnormal BP assessment at baseline and with ≥1 abnormal BP assessment after the start of treatment.
[e]Data for the aflibercept 8q8/3 and 8q8/5 groups were pooled.
[f]Denominator (n): 299.
[g]Demoninator (n): 587.
BP, blood pressure.

Serious Non-ocular TEAEs

	Aflibercept 2 mg pooled (n=857)	Aflibercept 8 mg pooled (n=1808)
Patients with ≥1 serious non-ocular TEAE, n (%)	**148 (17.3)**	**322 (17.8)**
Serious non-ocular TEAEs occurring in ≥10 patients in any group, n (%)		
Pneumonia	5 (0.6)	19 (1.1)
Myocardial infarction	4 (0.5)	14 (0.8)
Acute myocardial infarction	5 (0.6)	13 (0.7)
Osteoarthritis	4 (0.5)	11 (0.6)
Coronary artery disease	2 (0.2)	10 (0.6)

The incidence of serious non-ocular TEAEs was comparable in the pooled aflibercept 8 mg and 2 mg groups

Safety analysis set.

APTC Events and Treatment-Emergent Deaths

	Aflibercept 2 mg pooled (n=857)	Aflibercept 8 mg pooled (n=1808)
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)**

The incidence of APTC events and treatment-emergent deaths was comparable in the pooled aflibercept 8 mg and 2 mg groups

Safety analysis set.
[a]Events adjudicated as arterial thromboembolic events according to the APTC criteria.
APTC, Anti-Platelet Trialists' Collaboration.

Limitations

- This pooled analysis was limited to available safety data for aflibercept 8 mg from clinical trials with differing study designs and duration
  - **CANDELA (Phase 2):** 44-week data from 106 patients with nAMD
  - **PULSAR (Phase 3):** 96-week data from 1009 patients with nAMD
  - **PHOTON (Phase 2/3):** 96-week data from 658 patients with DME
  - **QUASAR (Phase 3):** 64-week data from 892 patients with MEfRVO

Conclusions

- In this pooled analysis of safety data for 2665 patients with nAMD, DME, or MEfRVO 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 in 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 in 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