

Comparable Safety Profile with Aflibercept 8 mg versus 2 mg: A Pooled Safety Analysis of the CANDELA, PULSAR, PHOTON, and QUASAR Trials

Ramin Khoramnia,^{1,2} on behalf of the CANDELA, PULSAR, PHOTON, and QUASAR study investigators

¹University Eye Clinic Heidelberg, Heidelberg, Germany; ²Department of Ophthalmology, University Hospital Carl Gustav Carus, TU Dresden, Dresden, Germany

Disclosures

- Ramin Khoramnia receives research funding from Alimera, Bayer, Chengdu Kanghong, Novartis, Opthea, and Roche; and serves as a speaker for AbbVie, Alimera, Apellis, Bayer, Heidelberg Engineering, Novartis, and Roche
- The CANDELA, PULSAR, PHOTON, and QUASAR studies were co-funded by Regeneron Pharmaceuticals, Inc. (Tarrytown, New York) and Bayer AG (Leverkusen, Germany). The study sponsors participated in the design and conduct of the respective studies, analysis of the data, and preparation of this abstract
- Study disclosures: These studies include research conducted on human patients; Institutional Review Board approval was obtained prior to study initiation
- Medical writing support was provided by Charlotte Head, BSc, ISMPP CMPPTM, of MEDiSTRAVA (Yardley, Pennsylvania), funded by Regeneron Pharmaceuticals, Inc. (Tarrytown, New York). Medical writing support for this encore was provided by Melanie Govender, PhD, ISMPP CMPPTM, of ApotheCom (London, UK) and funded by Bayer Consumer Care AG (Basel, Switzerland). All writing support was provided under the direction of the authors and in accordance with Good Publication Practice guidelines (*Ann Intern Med* 2022;175:1298–1304)
- Data were originally presented at the Retina World Congress 2026, Fort Lauderdale, Florida, May 14–17, 2026

Background and Methods

- Aflibercept 8 mg has demonstrated comparable efficacy and safety to aflibercept 2 mg in the pivotal PULSAR, PHOTON, and QUASAR trials^{1–5}
- 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

- Data from 4 multicenter, randomized clinical trials 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
- 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

	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

^aAll aflibercept 8 mg treatment groups from each trial were pooled. **DME**, diabetic macular edema; **MedDRA**, Medical Dictionary for Regulatory Activities; **MEfRVO**, macular edema following retinal vein occlusion; **nAMD**, neovascular age-related macular degeneration; **TEAE**, treatment-emergent adverse event. 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.

The Incidence of Ocular and Serious Ocular TEAEs was Comparable in the Pooled Aflibercept 8 mg and 2 mg Groups

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

No cases of occlusive retinal vasculitis were reported and the incidence of serious ocular TEAEs was comparably low in the pooled aflibercept 8 mg and 2 mg groups

Safety analysis set. ^aIncludes cataract, cataract cortical, cataract nuclear, cataract operation, cataract subcapsular, lenticular opacities, and posterior capsule opacifications, although not all terms met the ≥3% threshold. ^bIncludes cataract, cataract nuclear, and cataract subcapsular, although not all terms met the ≥2 patient threshold. IOP, intraocular pressure.

The Incidence of IOI-related Events was Low and Comparable in the Pooled Aflibercept 8 mg and 2 mg Groups

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

No cases of occlusive retinal vasculitis were reported and most IOI cases were non-serious and mild or moderate in severity

The Incidence of IOP- and Glaucoma-related TEAEs was Low and Comparable in the Pooled Aflibercept 8 mg and 2 mg Groups

	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	3.8 (2)	3.3 (11)	2.7 (18)	3.0 (5)	5.7 (28)	2.7 (8)	5.4 (32)
IOP ≥ 35 mmHg pre- or post-dose at any visit, % (n)	0	0	0.6 (2)	0.6 (4)	1.2 (2)	0.4 (2)	0.7 (2)	1.2 (7)

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

The rate of paracentesis procedures was low in the pooled aflibercept 8 mg (0.7%) and aflibercept 2 mg (0.2%) groups

Safety analysis set. ^aData for the aflibercept 8q12 and 8q16 groups were pooled. ^bData 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.

The Incidence of Non-ocular and Serious Non-ocular TEAEs was Comparable in the Pooled Aflibercept 8 mg and 2 mg Groups

	Aflibercept 2 mg pooled (n=857)	Aflibercept 8 mg pooled (n=1808)
Patients with ≥1 non-ocular TEAE, % (n)	68.3 (585)	69.2 (1252)
Non-ocular TEAEs occurring in ≥5% of patients in any group, % (n)		
COVID-19	10.0 (86)	12.8 (232)
Hypertension	6.5 (56)	9.4 (170)
Nasopharyngitis	6.9 (59)	7.0 (127)
Urinary tract infection	5.1 (44)	3.8 (68)
Patients with ≥1 serious non-ocular TEAE, % (n)	17.3 (148)	17.8 (322)
Serious non-ocular TEAEs occurring in ≥10 patients in any group, % (n)		
Pneumonia	0.6 (5)	1.1 (19)
Myocardial infarction	0.5 (4)	0.8 (14)
Acute myocardial infarction	0.6 (5)	0.7 (13)
Osteoarthritis	0.5 (4)	0.6 (11)
Coronary artery disease	0.2 (2)	0.6 (10)

The Incidence of Blood Pressure Elevations was Low and Comparable in the Pooled Aflibercept 8 mg and 2 mg Groups

	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)	17.0 (9)	11.3 (6)	12.2 (41)	13.0 (87)	30.9 (51)	31.5 (154)	9.0 (27 ^f)	8.9 (52 ^g)
Diastolic BP ≥110 mmHg and increase from baseline ≥10 mmHg, % (n)	1.9 (1)	0	1.2 (4)	0.4 (3)	2.4 (4)	3.7 (18)	0.7 (2 ^f)	2.4 (14 ^g)

^aPatients 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.
^bData for the aflibercept 8q12 and 8q16 groups were pooled.
^cPatients with a valid post-baseline BP value.
^dPatients without an abnormal BP assessment at baseline and with ≥1 abnormal BP assessment after the start of treatment.
^eData for the aflibercept 8q8/3 and 8q8/5 groups were pooled.
^fDenominator (n): 299.
^gDenominator (n): 587.
BP, blood pressure.

The Incidence of APTC Events and Treatment-emergent Deaths was Comparable in the Pooled Aflibercept 8 mg and 2 mg Groups

	Aflibercept 2 mg pooled (n=857)	Aflibercept 8 mg pooled (n=1808)
Patients with ≥ 1 APTC event,^a % (n)	3.4 (29)	3.0 (54)
Non-fatal myocardial infarction	1.3 (11)	1.2 (21)
Vascular death	1.3 (11)	0.9 (17)
Non-fatal stroke	0.8 (7)	0.9 (16)
Treatment-emergent deaths, % (n)	2.3 (20)	2.1 (38)

Safety analysis set.

^aEvents adjudicated as arterial thromboembolic events according to the APTC criteria.

APTC, Anti-Platelet Trialists' Collaboration.

Limitations and Conclusions

- This pooled analysis was limited to available safety data for aflibercept 8 mg from clinical trials with differing study designs and duration
 - **CANDELA**: 106 patients with nAMD
 - **PULSAR**: 1009 patients with nAMD
 - **PHOTON**: 658 patients with DME
 - **QUASAR**: 892 patients with MEfRVO
- In this pooled analysis of safety data for 2665 patients 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