A Pooled Analysis of the PULSAR and PHOTON Trials Through 96 Weeks: Minimal Impact of Aflibercept 8 mg and 2 mg on Intraocular Pressure Changes

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Disclosures

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  - **AL** is a consultant for AbbVie, Allergan, Apellis, Bayer, Biogen, Boehringer Ingelheim, Novartis, Ocular Therapeutix, Roche, and Santen; receives funding from Bayer, Novartis, and Roche. **DVD** is a consultant for AbbVie, Allergan, Apellis, Bayer, Biogen, Boehringer Ingelheim, Novartis, Ocular Therapeutix, Roche, and Santen; receives funding from Bayer, Novartis, and Roche. **PL** is a consultant for Aerie, Allergan, Apellis, Bausch & Lomb, Bayer, Biogen, Boehringer Ingelheim, Genentech, I-Care, Novartis, Outlook Therapeutics, and Roche. **SL**, **XZ**, **PMW**, and **LB** are employees of Bayer Consumer Care AG. **AJB**, **AM**, **AD**, **MH**, and **AP** are employees of Regeneron Pharmaceuticals, Inc. **KWC** is a former employee of Regeneron Pharmaceuticals, Inc. **MRB** is a consultant or in research for AbbVie Inc, Adverum Biotech, Alcon, Alimera, Allegro, Allergan, Annexon Biosciences, Apellis, Arctic Vision, Astellas, Bausch and Lomb, Biocryst, Biogen, Boehringer Ingelheim, CalciMedica, Celltrion, Cencora, Clearside Biomedical, Coherus Biosciences, EyeBio, EyePoint Pharma, Gemini Therapeutics, Genentech, Gyroscope Therapeutics, Harrow, Janssen, Kanghong/Vanotech, Kodiak Sciences, Novartis, NeuBase, Neurotech, Ocular Therapeutix, Oculis, Opthea, Outlook Therapeutics, Oxular, Oxurion, Palatin Technologies, Perfuse, Regeneron Pharmaceuticals, Inc., RegenxBio, ReNeuron, RevOpsis Therapeutics, Ribomic, Roche, Stealth Biotherapeutics, and Unity Biotechnology; and holds stock in NeuBase and Oxurion; has stock options with RevOpsis Therapeutics. **GG** has no financial disclosures to report. **MWS** is a consultant for Alkahest, Bayer, Biogen, Revena, Regeneron Pharmaceuticals, Inc., and Bayer; receives funding from Allergan, Kanghong, and Regeneron Pharmaceuticals, Inc. **CT** and **USO** are employees of Bayer AG
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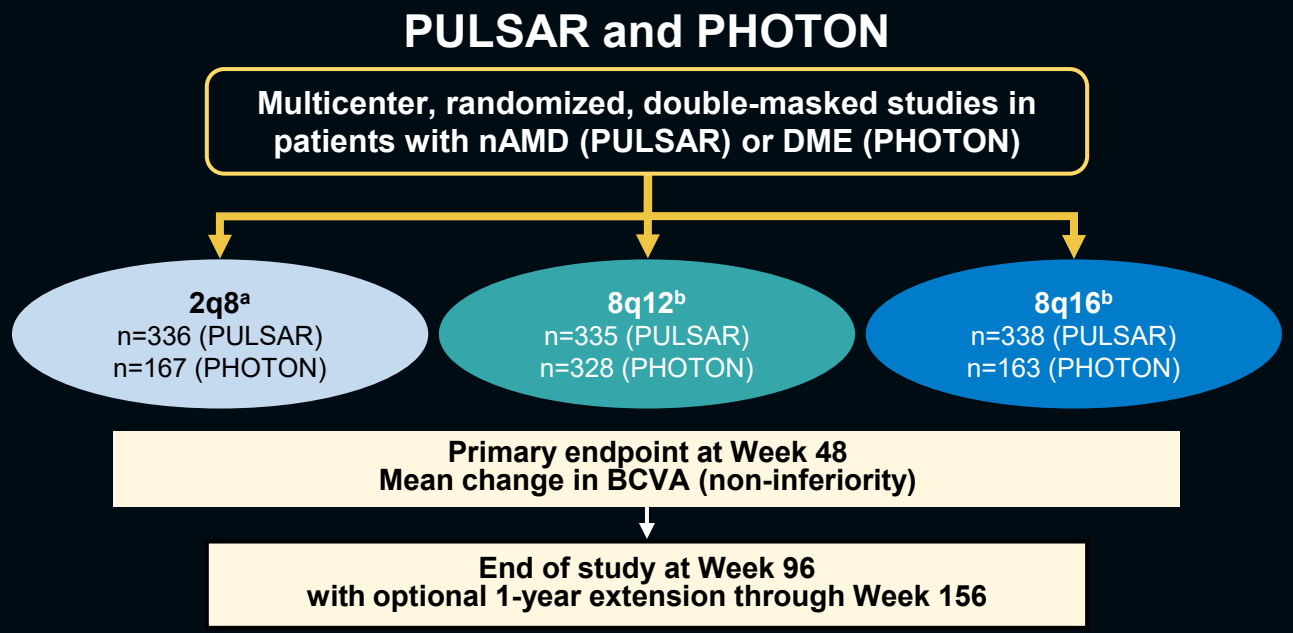
Objective and Methods

Objective

This analysis explored the potential effect of a higher injection volume with aflibercept 8 mg (70 uL) vs aflibercept 2 mg (50 uL) on IOP in the PULSAR and PHOTON trials through 96 weeks

Methods

- Data were pooled through Week 96 and IOP was measured at all visits as follows:
  - In **PULSAR**, measured pre-injection (bilaterally) and approximately 30 to 60 minutes after administration of study intervention (study eye only)
  - In **PHOTON**, measured pre-injection (bilaterally) by the masked investigator (or designee) and approximately 30 minutes after administration



Safety analysis set. [a]After 3 (PULSAR) or 5 (PHOTON) initial monthly injections. [b]After 3 initial monthly injections. **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; **DME**, diabetic macular edema; **IOP**, intraocular pressure; **nAMD**, neovascular age-related macular degeneration.

Sample Size, Baseline Demographics, and Aflibercept Exposure in the Pooled Safety Analysis

Overall, safety data for **1667 patients were evaluated**

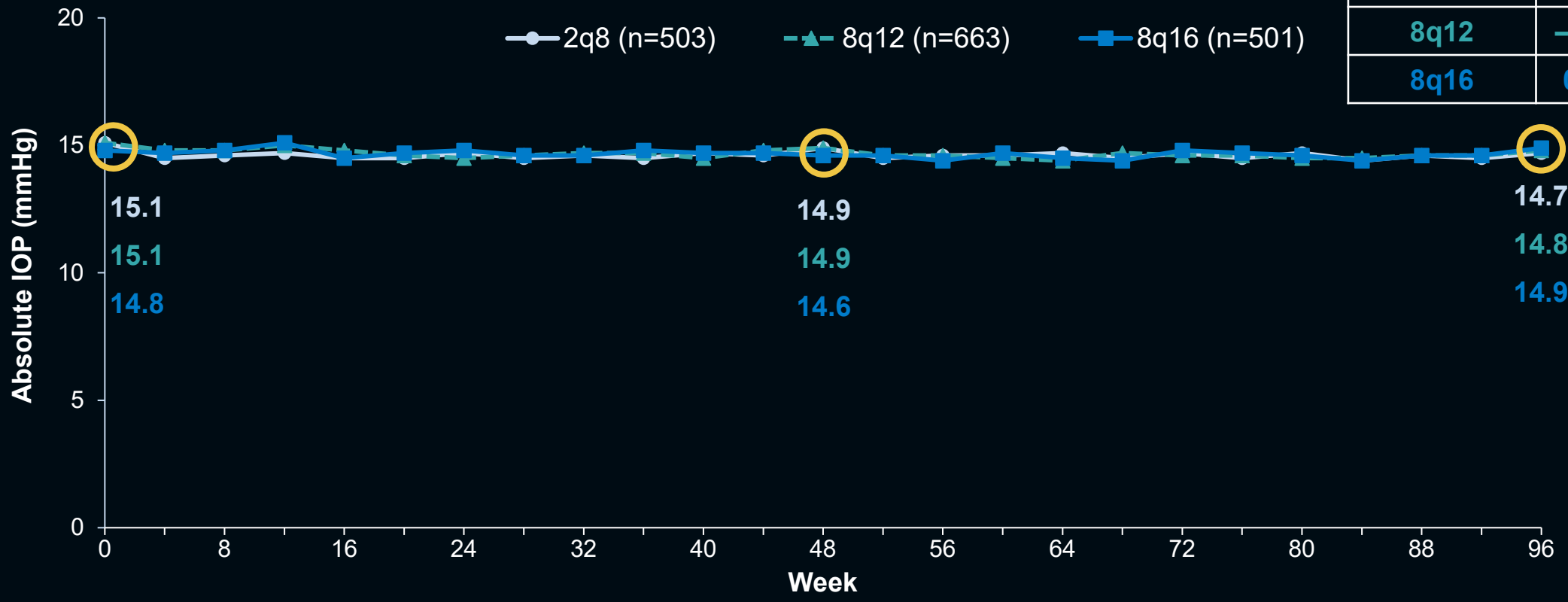
	Aflibercept 2 mg pooled	8q12	8q16	Aflibercept 8 mg pooled[a]
PULSAR, n	167	328	163	491
PHOTON, n	336	335	338	673
Total, n	503	663	501	1164

	Aflibercept 2 mg pooled (n=503)	Aflibercept 8 mg pooled[a] (n=1164)
Baseline demographics		
Female, n (%)	263 (52.3)	544 (46.7)
Age group, n (%) <65 years ≥65–<75 years ≥75 years	 137 (27.2) 180 (35.8) 186 (37.0)	 346 (29.7) 425 (36.5) 393 (33.8)
White, n (%)	361 (71.8)	875 (75.2)
Hispanic or Latino, n (%)	43 (8.5)	104 (8.9)
Aflibercept exposure		
Total number of injections	6159	9762

Safety analysis set. [a]Aflibercept 8q12 and 8q16 combined.

Absolute Pre-injection IOP Through Week 96

Change from baseline to Week 96	
2q8	–0.4 mmHg
8q12	–0.4 mmHg
8q16	0.1 mmHg



The mean pre-injection IOP values were comparable across treatment groups, with no sustained increase in IOP through Week 96

Safety analysis set through Week 96.

Pre-injection IOP in the Study Eye Through Week 96

	2q8	8q12	8q16	All 8 mg
Safety analysis set, n	503	663	501	1164
Pre-injection IOP ≥35 mmHg, n (%)[a]	1 (0.2)	2 (0.3)	0	2 (0.2)

The proportion of patients with pre-injection IOP ≥35 mmHg at any visit through Week 96 was very low and comparable across the treatment groups

[a]At any visit.

Post-injection IOP in the Study Eye Through Week 96

	2q8	8q12	8q16	All 8 mg
Safety analysis set, n	503	663	501	1164
Post-injection IOP ≥35 mmHg, n (%)[a]	3 (0.6)	3 (0.5)	1 (0.2)	4 (0.3)

The proportion of patients with post-injection IOP ≥35 mmHg at any visit through Week 96 was very low and comparable across the treatment groups

[a]At any visit.

Anterior Chamber Paracentesis in the Study Eye Through Week 96

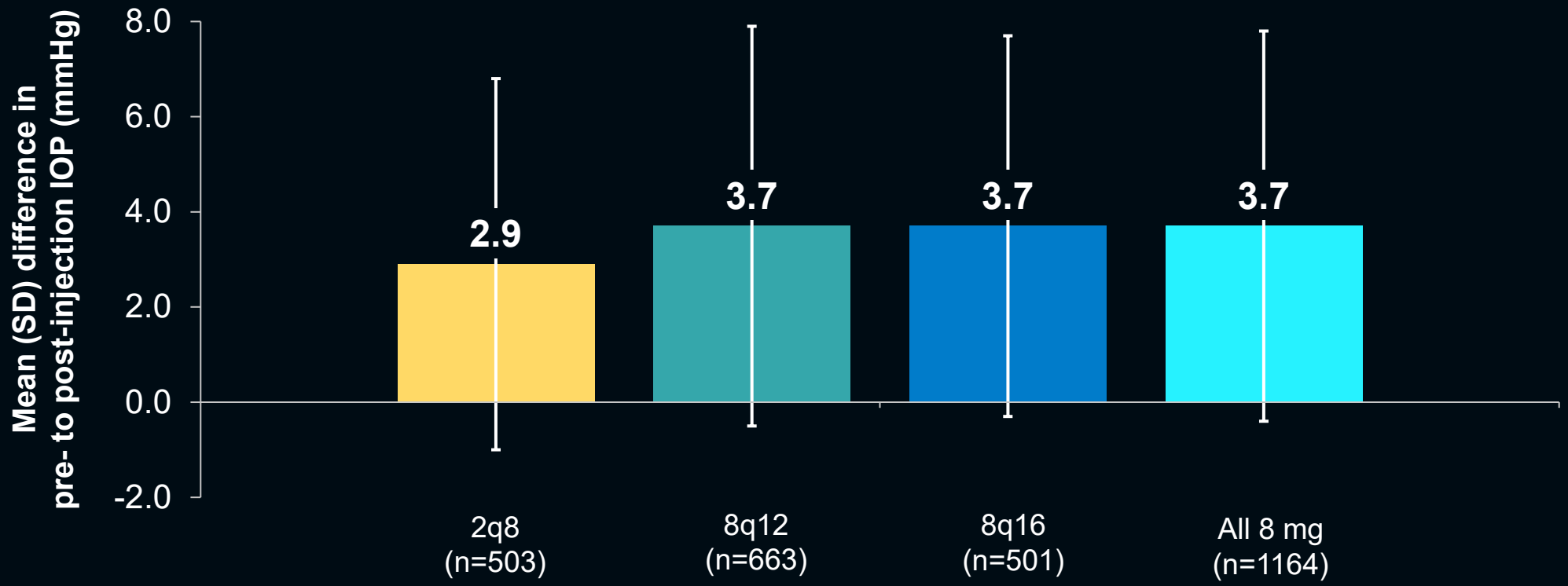
	2q8	8q12	8q16	All 8 mg
Number of patients requiring anterior chamber paracentesis/n (%)	0/503 (0)	4/663 (0.6)	1/501 (0.2)	5/1164 (0.4)
Number of events requiring anterior chamber paracentesis/number of active study eye injections (%)	0/6159 (0)	8/5920 (0.1)	1/3842 (<0.1)	9/9762 (<0.1)

The rates of anterior chamber paracentesis procedures performed through Week 96 were comparable across the treatment groups

Safety analysis set.

Difference in Pre-injection to Post-injection IOP in Study Eyes at Active Dosing Visits Through Week 96

Total number of active injections	6159	5920	3842	9762



The LS mean (95% CI) difference in pre- to post-injection IOP was comparable for patients in the combined All 8 mg and 2 mg groups with a difference of 0.83 (0.67, 0.99) mmHg

Safety analysis set through Week 96. **CI**, confidence interval; **LS,** least squares; **SD**, standard deviation.

IOP-related TEAEs Through Week 96

	2q8	8q12	8q16	All 8 mg
Safety analysis set, n	503	663	501	1164
Patients with ≥1 TEAE, n (%)	**22 (4.4)**	**31 (4.7)**	**22 (4.4)**	**53 (4.6)**
Angle closure glaucoma	1 (0.2)	1 (0.2)	1 (0.2)	2 (0.2)
Borderline glaucoma	0	1 (0.2)	1 (0.2)	2 (0.2)
Glaucoma	1 (0.2)	1 (0.2)	5 (1.0)	6 (0.5)
Intraocular pressure increased	17 (3.4)	21 (3.2)	13 (2.6)	34 (2.9)
Ocular hypertension	3 (0.6)	8 (1.2)	4 (0.8)	12 (1.0)
Open angle glaucoma	1 (0.2)	1 (0.2)	0	1 (<0.1)

TEAEs in the study eye. An IOP-related TEAE was defined based on the following preferred terms: “Angle closure glaucoma”, “Borderline glaucoma”, “Glaucoma”, “Glaucomatous optic neuropathy”, “Intraocular pressure increased”, “Ocular hypertension”, “Open angle glaucoma”, “Optic nerve cupping”, and “Trabeculoplasty”. **TEAE**, treatment-emergent adverse event.

Conclusions

Pre-injection and Post-injection IOP	• Pre-injection IOP values **remained consistent** over the 96-week period • The proportion of patients with **pre-injection IOP** and the proportion of patients with **post-injection IOP ≥35 mmHg** at any visit **through Week 96 was low and comparable** across the treatment groups
Anterior chamber paracentesis	• The rate of **anterior chamber paracentesis was comparable** across treatment groups and performed following **<0.1% of injections administered in the aflibercept 8 mg group**
Pre-injection to post-injection IOP differences	• The difference in LS mean change in pre-injection to post-injection IOP was **<1 mmHg between aflibercept 8 mg and 2 mg, and no clinically relevant differences** were observed
TEAEs	• The rate of **IOP-related TEAEs** such as “glaucoma", “IOP increased”, and “ocular hypertension” **were comparable across treatment groups**