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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Objective and Methods

Objective

This analysis evaluated the impact of aflibercept 8 mg (70 µl) and aflibercept 2 mg (50 µl) on intraocular pressure changes in the PULSAR and PHOTON trials through 96 weeks

Study design and IOP assessment in PULSAR and PHOTON trials

PULSAR and PHOTON

Multicenter, randomized, double-masked, non-inferiority studies in participants with nAMD (PULSAR) or DME (PHOTON)

- **2q8**[a]: n=336 (PULSAR), n=167 (PHOTON)
- **8q12**[b]: n=335 (PULSAR), n=328 (PHOTON)
- **8q16**[b]: n=338 (PULSAR), n=163 (PHOTON)

Primary endpoint at Week 48
Mean change in BCVA (non-inferiority)

↓

End of study at Week 96
with optional 1-year extension through Week 156

Pre-injection IOP assessment → Injection → Post-injection IOP assessment

Pre-injection IOP assessment (bilaterally)

Evaluated bilaterally before each active or sham injection

Post-injection IOP assessment (study eye only)

Study protocols recommended that IOP be measured at ~30 to 60 minutes (PULSAR) or ~30 minutes (PHOTON) after active or sham injection

The same method of measurement was used in each patient throughout the study (e.g., Goldmann applanation tonometry, Icare rebound tonometry, or Tono-pen™). On days when the study drug was administered, sites were permitted to follow their usual post-injection monitoring routine. Reported IOP was the last reading recorded before the patient was permitted to leave the study site. [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.

Baseline Demographics, Disease Characteristics, and Aflibercept Exposure

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

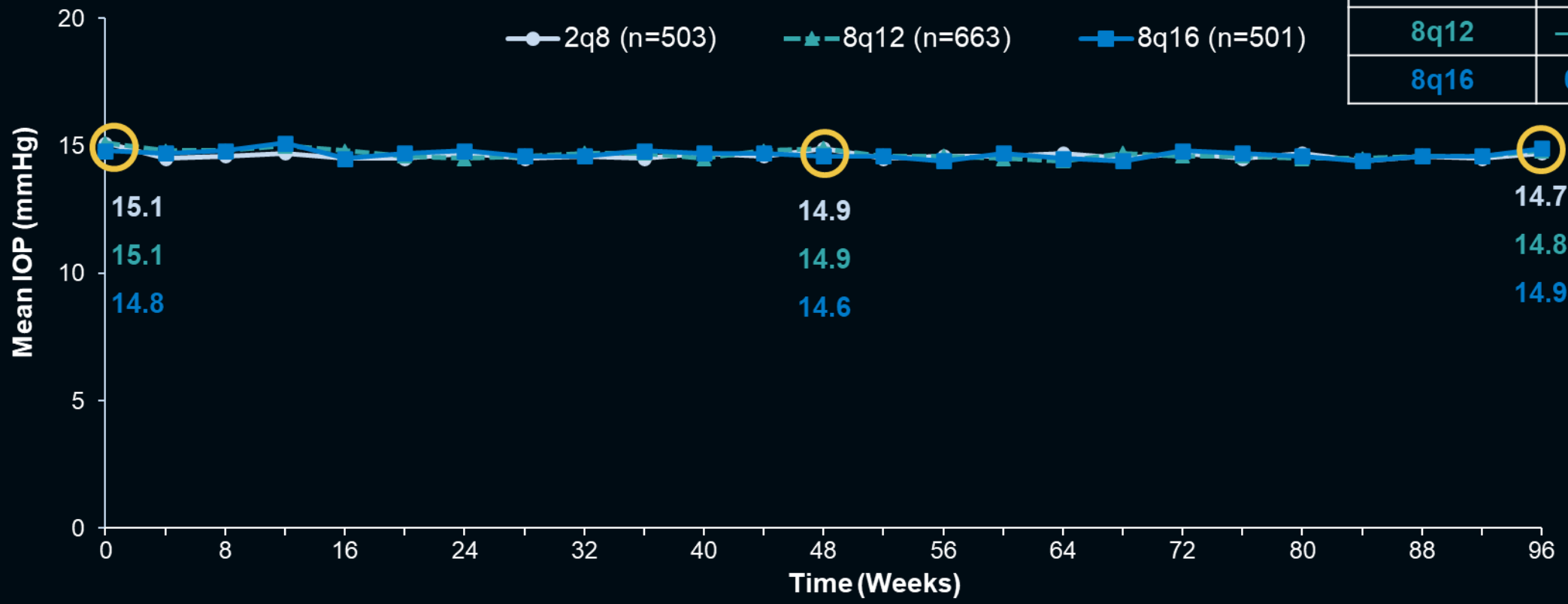
	Aflibercept 2 mg pooled	8q12	8q16	Aflibercept 8 mg pooled[a]
PULSAR, n	167	328	163	491
PHOTON, n	336	335	338	673
Total, n	503	663	501	1164

	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)
Baseline disease characteristics		
Mean (SD) IOP, mmHg	15.1 (3.0)	15.0 (3.2)
Medical history of IOP increase/glaucoma, n (%)	41 (8.2)	88 (7.6)
Aflibercept exposure		
Total number of injections	6159	9762

Safety analysis set. Data are in the study eye. [a]Aflibercept 8q12 and 8q16 combined. **SD**, standard deviation.

Mean 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.

Pre- or Post-injection IOP in the Study Eye Through Week 96

	2q8	8q12	8q16	All 8 mg
Safety analysis set, n	503	663	501	1164
Pre- or post-injection IOP ≥35 mmHg, n (%)[a]	4 (0.8)	5 (0.8)	1 (<0.1)	6 (0.1)
Pre-injection IOP ≥35 mmHg, n (%)[a]	1 (0.2)	2 (0.3)	0	2 (0.2)
Post-injection IOP ≥35 mmHg, n (%)[a]	3 (0.6)	3 (0.5)	1 (0.2)	4 (0.3)

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.

Anterior Chamber Paracentesis in the Study Eye Through Week 96

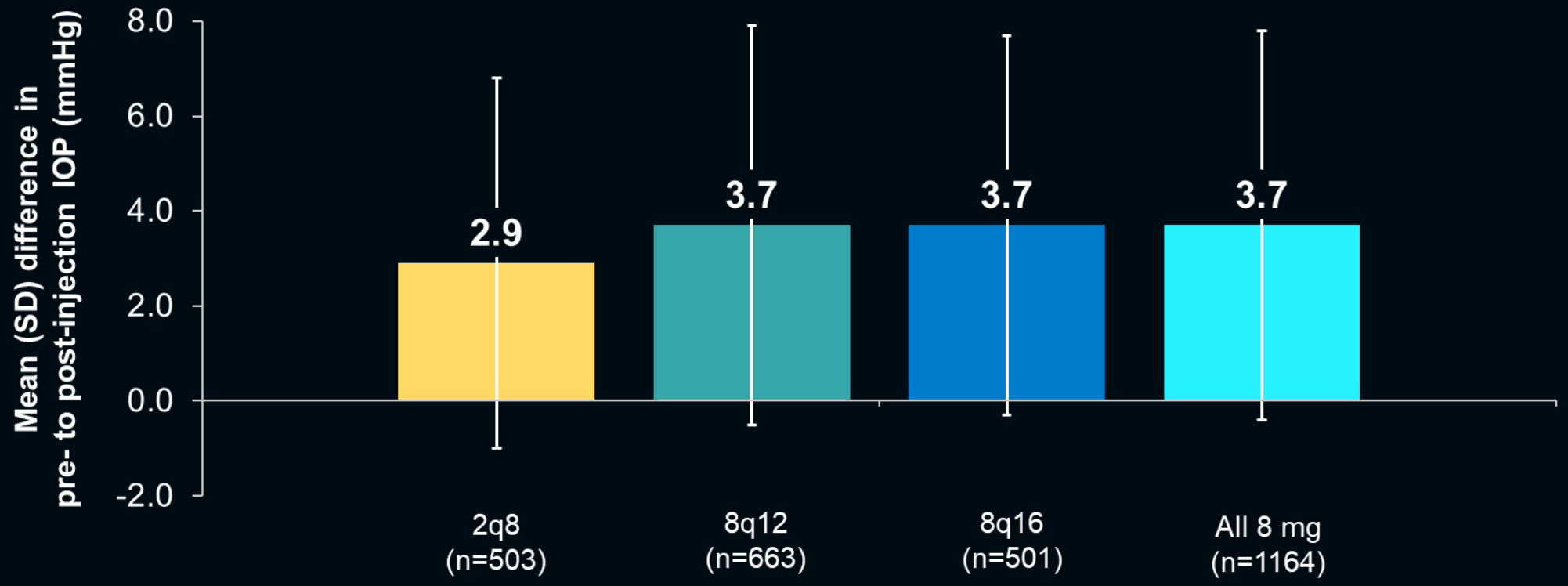
	2q8	8q12	8q16	All 8 mg
Number of patients requiring anterior chamber paracentesis/n (%)	0/503 (0)	4/663 (0.6)	1/501 (0.2)	5/1164 (0.4)
Number of events requiring anterior chamber paracentesis/number of active study eye injections (%)	0/6159 (0)	8/5920 (0.1)	1/3842 (<0.1)	9/9762 (<0.1)

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

Safety analysis set.

Differences 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 mmHg (0.67, 0.99)

Safety analysis set through Week 96. Active dosing visits. **CI**, confidence interval; **LS**, least squares.

IOP- and Glaucoma-related TEAEs in the Study Eye 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)

Safety analysis set. **TEAE**, treatment-emergent adverse event.

Conclusions

Pre-injection and Post-injection IOP	• Pre-injection IOP values **remained consistent** over the 96-week period • Few patients **(≤0.8%) had pre- or post-injection IOP ≥35 mmHg** at any visit with aflibercept 8 mg and aflibercept 2 mg
Anterior chamber paracentesis	• The rates of **anterior chamber paracentesis procedures were comparable** across treatment groups • The procedure was **performed following fewer than 0.1% of injections administered** in the aflibercept 8 mg group
Pre- to Post-injection IOP differences	• **No clinically relevant differences were observed in LS mean changes from pre- to post-injection IOP** of aflibercept 8 mg vs aflibercept 2 mg (0.83 mmHg [95% CI 0.67, 0.99])
TEAEs	• The incidence of **IOP-related TEAEs** such as “glaucoma", “IOP increased”, and “ocular hypertension” **was comparable across treatment groups**