Intraocular Pressure Outcomes With Aflibercept 8 mg and 2 mg in Patients With Diabetic Macular Edema: 156-Week Results From the PHOTON Extension Study

Poster #T12

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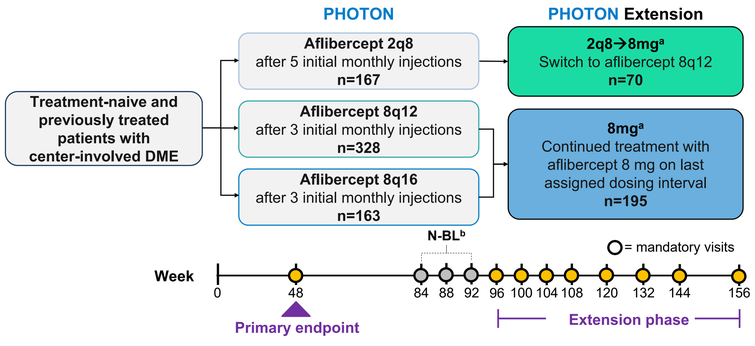
BACKGROUND & PURPOSE

- Aflibercept 8 mg demonstrated non-inferior best-corrected visual acuity (BCVA) gains with fewer injections compared to aflibercept 2 mg in patients with diabetic macular edema (DME) at Week 48 in the PHOTON trial (NCT04429503)[1]
  - Similar BCVA gains were maintained through 96 weeks[2]
- As the injection volume for aflibercept 8 mg is 70 µL compared with 50 µL for aflibercept 2 mg, the potential effect of a higher injection volume on intraocular pressure (IOP) and glaucoma-related outcomes was explored in an optional extension of the PHOTON trial through Week 156

METHODS

- In the PHOTON trial, treatment-naive and previously treated patients with center-involved DME were randomized 1:2:1 to receive aflibercept 2 mg every 8 weeks (2q8) after 5 initial monthly doses or aflibercept 8 mg every 12 weeks (8q12) or 16 weeks (8q16) after 3 initial monthly doses through 96 weeks
- Following completion of the PHOTON trial, patients had the option to participate in the PHOTON extension study in which those who previously received aflibercept 2q8 were switched to aflibercept 8 mg every 12 weeks at Week 96 (2q8→8mg group; n=70), and those who previously received aflibercept 8q12 or 8q16 continued to receive aflibercept 8 mg on their last assigned dosing interval (8mg group; n=195) (**Figure 1**)
- Fellow eyes could receive aflibercept 2-mg injections at the discretion of the study investigator through Week 96, or aflibercept 2 mg or 8 mg in the PHOTON extension

Figure 1. PHOTON Extension Trial Design



[a]Dosing visits were scheduled as needed based on individual dosing interval assignment. [b]Averaged over Weeks 84, 88, and 92. N-BL, new baseline.

IOP Assessment

- Bilateral IOP was measured at all study visits using either Goldmann applanation tonometry or Tono-pen. The same method of measurement was used in each patient throughout the study
- On days when the study drug was administered, sites were permitted to follow their usual post-injection monitoring routine. The study protocol recommended IOP be measured at approximately 30 minutes post-dose

Post Hoc Analysis

- IOP outcomes for study and fellow eyes in the extension safety analysis set were evaluated through Week 156
- In this analysis, fellow eyes were grouped based on study eye randomization in PHOTON. Both untreated and treated (only aflibercept was permitted) fellow eyes were included

REFERENCES

1. Brown DM et al. *Lancet*. 2024;403:1153–1163.
2. Do DV. Presented at: American Academy of Ophthalmology; November 3-6, 2023; San Francisco, CA.

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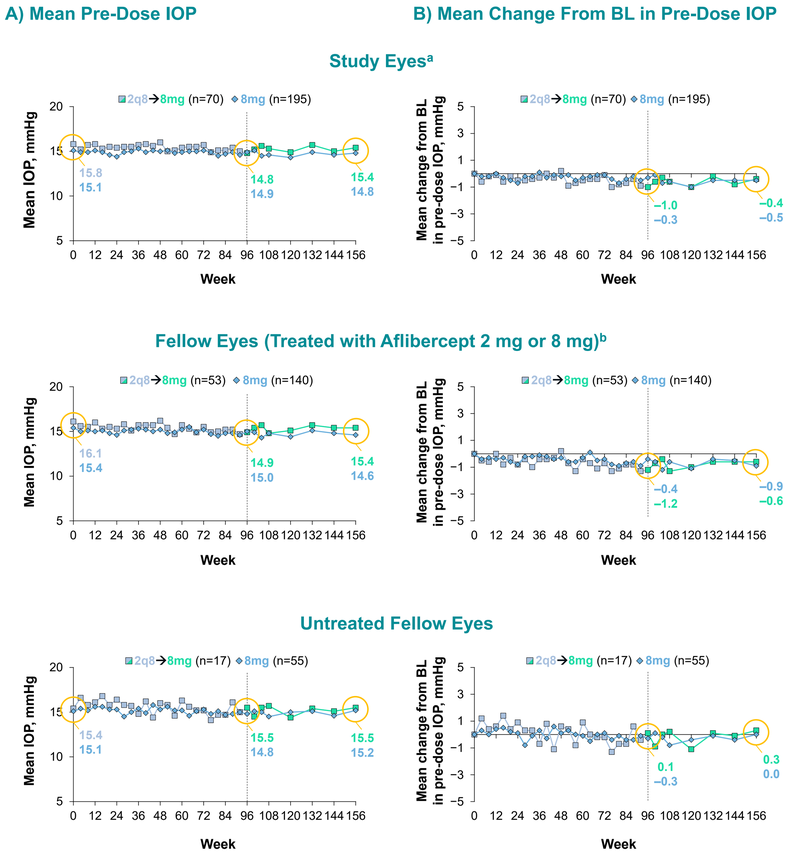
RESULTS

- Mean and mean change in pre-dose IOP values in study eyes in the 8mg group and the 2q8→8mg group were comparable through Week 156, and similar to baseline (BL)
  - In both treatment groups, mean changes in pre-dose IOP from BL by visit through Week 156 did not exceed ±1 mmHg in the study eye
  - These values were comparable in fellow eyes, irrespective of treatment with aflibercept (**Figure 2**)

Figure 2. (A) Mean Pre-Dose IOP and (B) Mean Change From BL in Pre-Dose IOP in Study and Fellow Eyes



Extension safety analysis set. Dashed lines at Week 96 indicate the end of the PHOTON trial, and the beginning of the PHOTON extension.
[a]Study eyes in the 2q8→8mg and 8mg groups received a mean of 18.6 and 12.6 injections, respectively. [b]At the discretion of the investigator, 75.7% of fellow eyes in the 2q8→8mg group and 71.8% of fellow eyes in the 8mg group received a mean of 14.6 and 14.0 injections, respectively, of aflibercept 2 mg or 8 mg. Fellow eye treatment was most commonly aflibercept 2 mg (only 10 patients received a total of 12 injections of aflibercept 8 mg in the fellow eye in the PHOTON extension).

- No study eyes had pre-dose IOP ≥25 mmHg at 2 consecutive visits or a pre-dose IOP value of ≥30 mmHg (**Table 1**)

Table 1. Cumulative Incidence of Patients Meeting Pre-Dose IOP Criteria Through Week 156

	Study eye				Fellow eye[a]			
	2q8→8mg (n=70)	8q12 (n=130)	8q16 (n=65)	8mg (n=195)	2q8→8mg (n=70)	8q12 (n=130)	8q16 (n=65)	8mg (n=195)
Pre-dose IOP ≥25 mmHg at 2 consecutive visits, %	0	0	0	0	1 (1.4)	2 (1.5)	0	2 (1.0)
Pre-dose IOP ≥30 mmHg at any visit, %	0	0	0	0	1 (1.4)	1 (0.8)	1 (1.5)	2 (1.0)

Extension safety analysis set.
Kaplan–Meier methodology was used to generate the data. If an assessment was missing at a specific visit, the visits preceding and following this visit were treated as consecutive visits. Eyes were counted only once in this analysis.
[a]Untreated or treated with aflibercept 8 mg or 2 mg.

- One study eye in the 2q8→8mg group had pre- or post-dose IOP ≥35 mmHg, which occurred before the extension phase. No study eyes in the 8mg group or fellow eyes met this criterion through Week 156
- The proportions of study and fellow eyes with a glaucoma-related history at BL were slightly higher with aflibercept 8 mg versus 2 mg (**Table 2**)
- The proportions of study and fellow eyes with or without glaucoma-related history at BL receiving a new or additional IOP-lowering agent(s) at any timepoint (including one-time administration) were low and comparable across treatment groups (**Table 2**)
  - Among eyes without glaucoma-related history, one study eye in the 2q8→8mg group received a new or additional IOP-lowering agent in the extension phase. One study eye in the 8q12 group and 4 fellow eyes received a new or additional IOP-lowering agent in the extension phase
  - Among eyes with glaucoma-related history, no study eyes in the 2q8→8mg group received a new or additional IOP-lowering agent in the extension phase. One study eye in the 8q12 group and 2 fellow eyes received a new or additional IOP-lowering agent in the extension phase

Table 2. Glaucoma-Related History at BL and IOP-Lowering Agents Through 156 Weeks

	Study eye				Fellow eye[a]			
	2q8→8mg (n=70)	8q12 (n=130)	8q16 (n=65)	8mg (n=195)	2q8→8mg (n=70)	8q12 (n=130)	8q16 (n=65)	8mg (n=195)
No glaucoma-related history at BL, n (%)[b]	66 (94.3)	118 (90.8)	56 (86.2)	174 (89.2)	66 (94.3)	117 (90.0)	55 (84.6)	172 (88.2)
Medical history of glaucoma/glaucoma suspect[c] AND/OR treatment with ≥1 IOP-lowering agent[d] at BL, n (%)	4 (5.7)	12 (9.2)	9 (13.8)	21 (10.8)	4 (5.7)	13 (10.0)	10 (15.4)	23 (11.8)
Eyes without glaucoma-related history that received a new or additional IOP-lowering agent(s) through Week 156, n/N	3/66	4/118	1/56	5/174	2/66	6/117	0	6/172
Eyes with glaucoma-related history that received a new or additional IOP-lowering agent(s) through Week 156, n/N	2/4	2/12	2/9	4/21	0	3/13	2/10	5/23

Extension safety analysis set.
[a]Untreated or treated with aflibercept 8 mg or 2 mg. [b]No medical history of glaucoma/glaucoma suspect or not receiving an IOP-lowering agent at BL. [c]Defined as a medical history of glaucoma/glaucoma suspect (glaucoma, open-angle glaucoma, borderline glaucoma, ocular hypertension, angle closure glaucoma, glaucomatous optic disc atrophy, optic nerve cupping, trabeculoplasty, or IOP increased) or receiving an IOP-lowering agent at BL. [d]Beta blockers, prostaglandin analogues, carbonic anhydrase inhibitors, or other anti-glaucoma preparations.

- Only 2 study eyes in the 8mg group received an anterior chamber paracentesis through Week 156; both were performed in Year 2 of the PHOTON trial. No study eyes in the 2q8→8mg group, and no fellow eyes received an anterior chamber paracentesis through Week 156 (**Table 3**)
- The only other IOP-lowering procedure performed in study eyes was an iridotomy (1 in the 8q12 group and 1 in the 8q16 group)
  - One fellow eye received an iridotomy and 1 fellow eye received a trabeculectomy

Table 3. Anterior Chamber Paracentesis Procedures[a] Through Week 156

	Study eye				Fellow eye[b]			
	2q8→8mg (n=70)	8q12 (n=130)	8q16 (n=65)	8mg (n=195)	2q8→8mg (n=70)	8q12 (n=130)	8q16 (n=65)	8mg (n=195)
Eyes receiving anterior chamber paracentesis, n (%)	0	1 (0.8)	1 (0.5)	2 (1.0)	0	0	0	0

Extension safety analysis set.
[a]Ocular treatment-emergent surgeries in the study or fellow eye. [b]Untreated or treated with aflibercept 8 mg or 2 mg.

CONCLUSIONS

- In patients with DME, pre-dose IOP values in the study eye were similar through Week 156 across the aflibercept 8-mg and 2-mg treatment groups and between study eyes and fellow eyes, regardless of treatment with aflibercept 8 mg or 2 mg
- The proportions of study and fellow eyes with and without glaucoma-related history requiring IOP-lowering medications were low across all treatment groups through Week 156
- Only 2 study eyes receiving aflibercept 8 mg (1 in the 8q12 group and 1 in the 8q16 group) required anterior chamber paracentesis through Week 156
- Despite a 70-µL injection volume, no long-term IOP adverse effects were seen through Week 156 with aflibercept 8 mg versus 2 mg (50 µL)

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