Intraocular Pressure Outcomes With Aflibercept 8 mg and 2 mg in Patients With Diabetic Macular Edema Through Week 96 of the Phase 2/3 PHOTON Trial

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BACKGROUND & PURPOSE

- Aflibercept 8 mg demonstrated non-inferior visual outcomes compared with aflibercept 2 mg with fewer injections at Week 96 in patients with diabetic macular edema (DME) from the PHOTON trial (NCT04429503)[1,2]
- As aflibercept 8 mg is administered in a 70-µL injection volume versus a 50-µL injection volume for aflibercept 2 mg, the potential effect of a higher injection volume on intraocular pressure (IOP) should be further explored
- This analysis evaluated IOP and glaucoma-related outcomes in eyes receiving aflibercept 8 mg or 2 mg for DME through 96 weeks

METHODS

- In the PHOTON study, eligible patients with DME were randomized 1:2:1 to receive aflibercept 8 mg every 12 or 16 weeks after 3 initial monthly doses (8q12 or 8q16; 70 µL) or aflibercept 2 mg every 8 weeks after 5 initial monthly doses (2q8; 50 µL) (**Figure 1**)
- Fellow eyes could receive aflibercept 2-mg injections at the discretion of the study investigator

Figure 1. PHOTON Study Design

Multicenter, randomized, double-masked study in patients with DME[a]
Randomized 1 (2q8) : 2 (8q12) : 1 (8q16)

- **2q8**: Aflibercept 2 mg every 8 weeks after 5 initial monthly injections (50 µL) n=167
- **8q12**: 8 mg every 12 weeks after 3 initial monthly injections (70 µL) n=328
- **8q16**: 8 mg every 16 weeks after 3 initial monthly injections (70 µL) n=163

Fellow eyes could receive aflibercept 2 mg at the discretion of the investigator

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

[a]Treatment naive and previously treated.
BCVA, best-corrected visual acuity.

IOP Assessment in the PHOTON Trial

- 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

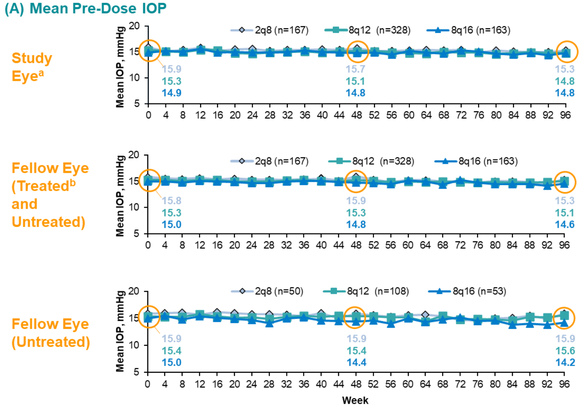
Post Hoc Analysis

- IOP outcomes for study and fellow eyes in the safety analysis set were evaluated through Week 96
- In this analysis, fellow eyes were grouped based on study eye randomization. Both untreated and treated (only aflibercept 2 mg was permitted) fellow eyes were included
  - Through Week 96, fellow eye injections with aflibercept 2 mg were reported in 70.1%, 67.1%, and 67.5% of patients in the 2q8, 8q12, and 8q16 study eye randomization groups, respectively

RESULTS

- Mean pre-dose IOP values were similar through Week 96 in study and fellow eyes (treated with aflibercept 2 mg or untreated), suggesting no drift toward increased IOP over time (**Figure 2A**)
- Similarly, mean change in pre-dose IOP from baseline (BL) was comparable in study and untreated fellow eyes, further supporting that there was no drift toward increased IOP over time (**Figure 2B**)

Figure 2. (A) Mean Pre-Dose IOP and (B) Mean Change in Pre-Dose IOP From BL in Study and Fellow Eyes Through Week 96



Safety analysis set.
[a]Study eyes in 2q8, 8q12, and 8q16 groups received a mean of 14.0, 9.0, and 8.0 injections, respectively, through Week 96.
[b]2-mg treated fellow eyes in 2q8, 8q12, and 8q16 groups received a mean of 10.0, 9.4, and 10.8 injections, respectively, through Week 96.

- The cumulative incidence of an increase in pre-dose IOP of ≥25 mmHg at 2 consecutive visits or of a pre-dose IOP ≥30 mmHg at any visit was low (**Table 1**)
  - Outcomes in treated and untreated fellow eyes were comparable with those for study eyes

Table 1. Cumulative Incidence of Patients Meeting Pre-Dose IOP Criteria Through Week 96

	Study eye			Fellow eye[a]	
	2q8 (n=167)	8q12 (n=328)	8q16 (n=163)	2-mg treated (n=447)	Untreated (n=211)
Pre-dose IOP ≥25 mmHg at 2 consecutive visits, %	0.0	0.0	0.7	0.9	0.5
Pre-dose IOP ≥30 mmHg at any visit, %	0.0	0.7	0.0	0.3	0.5

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]2-mg treated and untreated fellow eyes; all study eye randomization arms were combined.

- The proportion of study and fellow eyes with IOP ≥35 mmHg pre- or post-injection at any visit was low and comparable across treatment groups (**Table 2**)

Table 2. IOP Through Week 96 in Study and Fellow Eyes

	Study eye			Fellow eye[a]		
	2q8 (n=167)	8q12 (n=328)	8q16 (n=163)	2q8 (n=167)	8q12 (n=328)	8q16 (n=163)
IOP ≥35 mmHg pre-or post-injection at any visit, n (%)	2 (1.2)	2 (0.6)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)

Safety analysis set.
[a]2-mg treated and untreated fellow eyes.

- The proportions of eyes with glaucoma-related history were comparable in study and fellow eyes and across treatment groups (**Table 3**)
- When looking at eyes either with or without glaucoma-related history at BL, the proportions of eyes that received a new IOP-lowering agent at any timepoint (including one-time administration) were low and comparable across all treatment arms in study and fellow eyes (**Table 3**)

Table 3. Glaucoma-Related History at BL and IOP-Lowering Agents Through Week 96

	Study eye			Fellow eye[a]		
	2q8 (n=167)	8q12 (n=328)	8q16 (n=163)	2q8 (n=167)	8q12 (n=328)	8q16 (n=163)
Eyes with medical history of glaucoma/glaucoma suspect[b] AND/OR receiving ≥1 IOP-lowering agent[c] at BL, n (%)	13 (7.8)	26 (7.9)	13 (8.0)	13 (7.8)	33 (10.1)	16 (9.8)
Eyes with no glaucoma-related history at BL, n (%)[d]	154 (92.2)	302 (92.1)	150 (92.0)	154 (92.2)	295 (90.0)	147 (90.2)
Eyes with glaucoma-related history that received a new IOP-lowering agent(s) through Week 96, n/N (%)	3/13 (23.1)	3/26 (11.5)	2/13 (15.4)	1/13 (7.7)	4/33 (12.1)	2/16 (12.5)
Eyes with no glaucoma-related history that received a new IOP-lowering agent(s) through Week 96, n/N (%)	5/154 (3.3)	8/302 (2.6)	5/150 (3.3)	3/154 (1.9)	6/295 (2.0)	2/147 (1.4)

Safety analysis set.
Glaucoma-related history was defined as a medical history of glaucoma/glaucoma suspect and/or receiving ≥1 IOP-lowering agent(s) at BL in study and/or fellow eyes.
[a]2-mg treated and untreated fellow eyes.
[b]Medical history of glaucoma/glaucoma suspect or on an IOP-lowering agent(s) at BL: glaucoma/glaucoma suspect terms—glaucoma, open-angle glaucoma, borderline glaucoma, ocular hypertension, angle-closure glaucoma, glaucomatous optic disc atrophy, optic nerve cupping, trabeculoplasty, IOP increased.
[c]IOP-lowering agents: beta blocking agents, prostaglandin analogues, carbonic anhydrase inhibitors, or other anti-glaucoma preparations.
[d]No medical history of glaucoma/glaucoma suspect or receiving ≥1 IOP-lowering agent(s) at BL: glaucoma/glaucoma suspect terms—glaucoma, open-angle glaucoma, borderline glaucoma, ocular hypertension, angle-closure glaucoma, glaucomatous optic disc atrophy, optic nerve cupping, trabeculoplasty, IOP increased.

- The proportion of study and fellow eyes receiving an anterior chamber paracentesis through Week 96 was low and comparable across treatment groups (**Table 4**)
- The only other IOP-lowering procedure reported through Week 96 was iridotomy in 1 patient (in both the study and fellow eye) in the 8q12 group

Table 4. Anterior Chamber Paracentesis Procedures[a] in All Patients Through Week 96

	Study eye			Fellow eye[b]		
	2q8 (n=167)	8q12 (n=328)	8q16 (n=163)	2q8 (n=167)	8q12 (n=328)	8q16 (n=163)
Eyes receiving anterior chamber paracentesis through Week 96, n (%)	0 (0.0)	3 (0.9)	1 (0.6)	1 (0.6)	1 (0.3)	0 (0.0)

- Two patients in the 8q12 group received 1 paracentesis in the study eye only
- One patient in the 8q12 group received multiple paracentesis in both the study and fellow eyes
- One patient in the 8q16 group received 1 paracentesis in the study eye only
- One patient in the 2q8 group received 1 paracentesis in the fellow eye only

Safety analysis set.
[a]Ocular treatment-emergent surgeries in study/fellow eye related to IOP lowering.
[b]2-mg treated and untreated fellow eyes.

CONCLUSIONS

- Despite a 70-µL injection volume, no long-term IOP adverse effects were seen through Week 96 with aflibercept 8 mg versus 2 mg (50 µL)
  - In patients with DME, pre-dose IOP values in the study eye were similar through Week 96 across treatment groups
  - Pre-dose IOP values were similar through Week 96 between study eyes and fellow eyes (treated with aflibercept 2 mg and untreated)
  - Proportions of study and fellow eyes with and without glaucoma-related history requiring IOP-lowering medications were low across all treatment groups through Week 96
  - Only 4 study eyes receiving aflibercept 8 mg and 2 fellow eyes required anterior chamber paracentesis through Week 96

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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