# Intraocular Pressure Outcomes With Intravitreal Injection of Aflibercept 8 mg and 2 mg in Patients With Diabetic Macular Edema Through Week 48 of the Phase 2/3 PHOTON Trial

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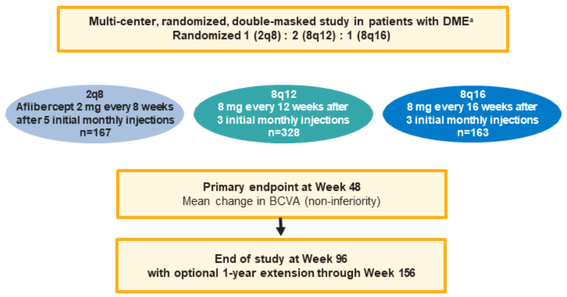
## BACKGROUND & PURPOSE

- Aflibercept 8 mg demonstrated non-inferior visual outcomes compared with aflibercept 2 mg with fewer injections at Week 48 in patients with diabetic macular edema (DME) from the PHOTON trial (NCT04429503)[1]
- 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) needs to be further characterized
- This analysis evaluated IOP and glaucoma-related outcomes in eyes receiving aflibercept 8 mg or 2 mg for DME

## 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 monthly doses (8q12 or 8q16, 70 µL) or aflibercept 2 mg every 8 weeks after 5 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




[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

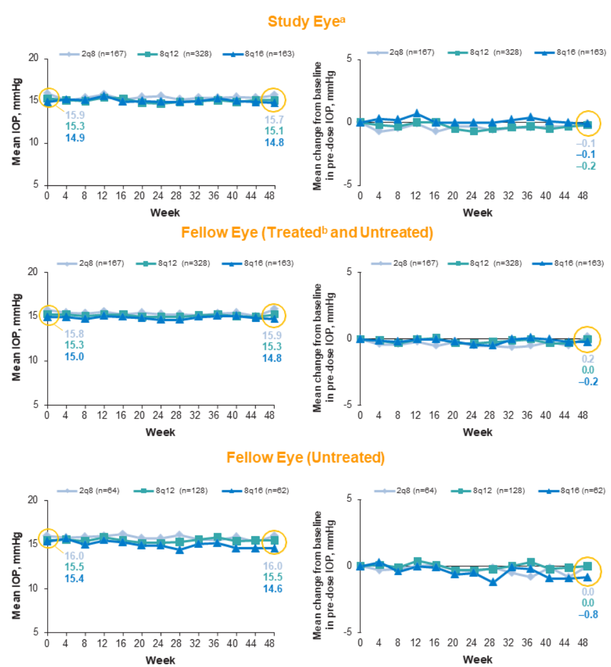
### Post Hoc Analysis

- IOP outcomes for study and fellow eyes in the safety analysis set were evaluated through Week 48
- In this analysis, fellow eyes were grouped based on study eye randomization. Both untreated and treated fellow eyes were included
  - Through Week 48, 61.7%, 61.0%, and 62.0% of patients in the 2q8, 8q12, and 8q16 groups, respectively, received aflibercept 2 mg injections in the fellow eye, with a mean of 6.4, 5.8, and 6.5 injections, respectively.

## RESULTS

- Mean pre-dose IOP values were similar through Week 48 in study and fellow eyes (treated or untreated with aflibercept 2 mg), 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 48




Safety analysis set.
[a]Study eyes in 2q8, 8q12, and 8q16 groups received a mean of 7.7, 5.7, and 4.9 injections, respectively, through Week 48.
[b]Treated fellow eyes in 2q8, 8q12, and 8q16 groups received a mean of 6.4, 5.8, and 6.5 injections, respectively, through Week 48.

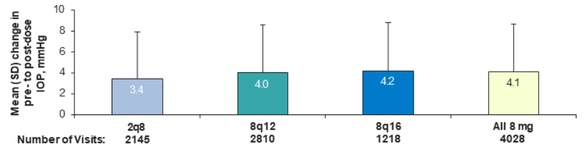
- The cumulative incidence of an increase in pre-dose IOP of ≥5 mmHg from baseline at 2 consecutive visits was low and similar in study and fellow eyes, as well as across treatment groups (**Table 1**)
  - No study eyes had pre-dose IOP ≥25 mmHg at 2 consecutive visits. One study eye in the 8q12 group had a value of pre-dose IOP ≥30 mmHg
  - Several fellow eyes had pre-dose IOP ≥25 mmHg at 2 consecutive visits
  - There was 1 fellow eye that met the criteria for both 2 consecutive visits with pre-dose IOP ≥25 mmHg and a value of pre-dose IOP ≥30 mmHg
- Mean change in pre-dose to post-dose IOP in study eyes at active dosing visits was similar across treatment groups (**Figure 3**)

### Table 1. Cumulative Incidence of Eyes Meeting Pre-dose IOP Analysis Criteria Through Week 48

| | Study Eye | | | Fellow Eye[a] | | |
|---|---|---|---|---|---|---|
| | 2q8 (n=167) | 8q12 (n=328) | 8q16 (n=163) | 2q8 (n=167) | 8q12 (n=328) | 8q16 (n=163) |
| Pre-dose IOP increase of ≥5 mmHg from baseline at 2 consecutive visits, % | 8.9 | 10.9 | 13.2 | 8.7 | 12.8 | 10.7 |
| Pre-dose IOP ≥25 mmHg at 2 consecutive visits, % | 0.0 | 0.0 | 0.0 | 1.2 | 0.7[b] | 0.0 |
| Pre-dose IOP ≥30 mmHg at any visit, % | 0.0 | 0.3[c] | 0.0 | 0.6 | 0.0 | 0.0 |

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]Treated and untreated fellow eyes.
[b]History of glaucoma or ocular hypertension.
[c]History of ocular hypertension in the fellow eye.

### Figure 3. Mean Change in Pre-dose to Post-dose IOP[a] in Study Eyes at Active Dosing Visits




Safety analysis set: 2q8, n=167; 8q12, n=328; 8q16, n=163; all 8 mg, n=491.
If there were signs or symptoms before 30 minutes that may have indicated a higher IOP increase such as pain or vision loss, then IOP would have been measured sooner and managed appropriately at the discretion of the investigator, including by administration of IOP-lowering agents or procedures.
[a]Reported post-dose IOP was the last reading recorded before the patient was permitted to leave the study site. SD, standard deviation.

### Table 2. Glaucoma-related History at Baseline and IOP-lowering Agents in Eyes without Glaucoma-related History

| | 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 baseline, n (%) | 12 (7.2) | 26 (7.9) | 13 (8.0) | 12 (7.2) | 32 (9.8) | 16 (9.8) |
| Eyes with no glaucoma-related history at baseline, n (%)[b] | 155 (92.8) | 302 (92.1) | 150 (92.0) | 155 (92.8) | 296 (90.2) | 147 (90.2) |
| Eyes with no glaucoma-related history who were started on an IOP-lowering agent(s) through Week 48, n (% of row above) | 3 (1.9) | 4 (1.3) | 1 (0.7) | 2 (1.3) | 3 (1.0) | 0 (0.0) |

**Three unique patients (5 eyes) without glaucoma-related history in the 2q8 arm started an IOP-lowering agent:**
- Two patients were started and continued on an IOP-lowering agent through Week 48 in both the study and fellow eyes
- One patient required an IOP-lowering agent in the study eye only, which was started and stopped before Week 48 of the study

**Four unique patients (7 eyes) without glaucoma-related history in the 8q12 arm started and continued on an IOP-lowering agent:**
- Three patients required an IOP-lowering agent in both the fellow and study eyes
- One patient required an IOP-lowering agent in the study eye only

Safety analysis set.
Glaucoma-related history was defined as a medical history of glaucoma/glaucoma suspect and/or receiving an IOP-lowering agent(s) at baseline in study and/or fellow eyes.
[a]Treated and untreated fellow eyes.
[b]Medical history of glaucoma/glaucoma suspect or on an IOP-lowering agent(s) at baseline: glaucoma/glaucoma suspect terms-glaucoma, open angle glaucoma, borderline glaucoma, ocular hypertension, angle closure glaucoma, glaucomatous optic disc atrophy, optic nerve cupping, trabeculoplasty, intraocular pressure increased.
[c]IOP-lowering agents: beta blocking agents, prostaglandin analogues, carbonic anhydrase inhibitors, or other anti-glaucoma preparations; there was 1 patient on an IOP-lowering agent at baseline without a recorded history of glaucoma/glaucoma suspect.

- The proportions of eyes with glaucoma-related history at baseline were comparable across treatment groups (**Table 2**)
- Few patients without glaucoma-related history required an IOP-lowering agent(s) through Week 48 (**Table 2**)
- Anterior chamber paracentesis was the only IOP-lowering procedure reported through Week 48 (**Table 3**)
  - Two study eyes in the 8q12 group and 1 fellow eye in the 2q8 group received an anterior chamber paracentesis with/without IOP-lowering medications through Week 48
  - All of these patients continued the study

### Table 3. Eyes Requiring IOP-lowering Procedures[a] Through Week 48

| | 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 with or without an IOP-lowering agent[c] through Week 48, n (%) | 0 (0.0) | 2 (0.6) | 0 (0.0) | 1 (0.6) | 0 (0.0) | 0 (0.0) |

Safety analysis set.
[a]Ocular treatment-emergent surgeries in study/fellow eye related to IOP lowering.
[b]Treated and untreated fellow eyes.
[c]IOP-lowering agents: beta-blocking agents, prostaglandin analogues, carbonic anhydrase inhibitors, or other anti-glaucoma preparations.

## CONCLUSIONS

- In patients with DME, pre-dose IOP values in the study eye were similar through Week 48 across treatment groups and between study eyes and fellow eyes (treated and untreated with aflibercept 2 mg)
- No clinically relevant differences in change in pre- to post-dose IOP were observed across treatment groups through Week 48
- The proportions of study and fellow eyes without glaucoma-related history requiring IOP-lowering medications were low across all treatment groups through Week 48
- Only 3 eyes required anterior chamber paracentesis, the only reported IOP-lowering procedure through Week 48
- Despite a 70-µL injection volume, no long-term IOP adverse effects were seen through Week 48 with aflibercept 8 mg versus 2 mg (50 µL)

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## REFERENCES

1. Brown DM, et al. *The Lancet*. 2024;403(10432):1153–1163.

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