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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Disclosures

DME

- Dr. Do is a consultant to Boehringer Ingelheim, Genentech, Kodiak Sciences, Kriya, and Regeneron Pharmaceuticals, Inc.; has received research funding from Boehringer Ingelheim, Genentech, Kriya, and Regeneron Pharmaceuticals, Inc.; and has stock options from Kodiak Sciences
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- Study disclosures: This study includes research conducted on human patients. Institutional Review Board approval was obtained prior to study initiation

Background

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- Aflibercept 8 mg demonstrated non-inferior visual outcomes compared to aflibercept 2 mg with fewer injections at Week 48 in patients with DME from the PHOTON trial[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 IOP needs to be further characterized
  - Through Week 48, 62% of fellow eyes received aflibercept 2 mg at the discretion of the study investigator

This analysis evaluated IOP and glaucoma-related outcomes in eyes receiving aflibercept 8 mg or 2 mg for DME

DME, diabetic macular edema; IOP, intraocular pressure.

1. Brown DM. Intravitreal aflibercept injection 8 mg for DME: results from the phase 2/3 PHOTON trial. Presented at: American Academy of Ophthalmology; September 30, 2022; Chicago, IL.

PHOTON Study Design

Multi-center, 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 naïve and previously treated.
BCVA, best-corrected visual acuity.

Glaucoma-related History at Baseline

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	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)

The proportions of eyes **with glaucoma-related history** were comparable across treatment groups

Safety analysis set.
[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 one patient on an IOP-lowering agent at baseline without a recorded history of glaucoma/glaucoma suspect.

Methods

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IOP Assessment in the PHOTON Trial

- Bilateral IOP was measured at all study visits; the same method of measurement was used in each patient throughout the study[a]
  - On days when study drug was administered, sites were permitted to follow their usual post-injection monitoring routine. The study protocol recommended that IOP be measured at approximately 30 minutes post-dose

Post Hoc Analysis

- IOP outcomes for study eyes 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 (only aflibercept 2 mg was permitted) fellow eyes were included
  - Through Week 48, fellow eye injections with aflibercept 2 mg were reported in 61.7%, 61.0%, and 62.0% of patients in the 2q8, 8q12, and 8q16 groups, respectively

[a]IOP was measured using either Goldmann applanation tonometry or Tono-pen™.

Mean Pre-dose IOP Values in Study and Fellow Eyes Were Similar Through Week 48

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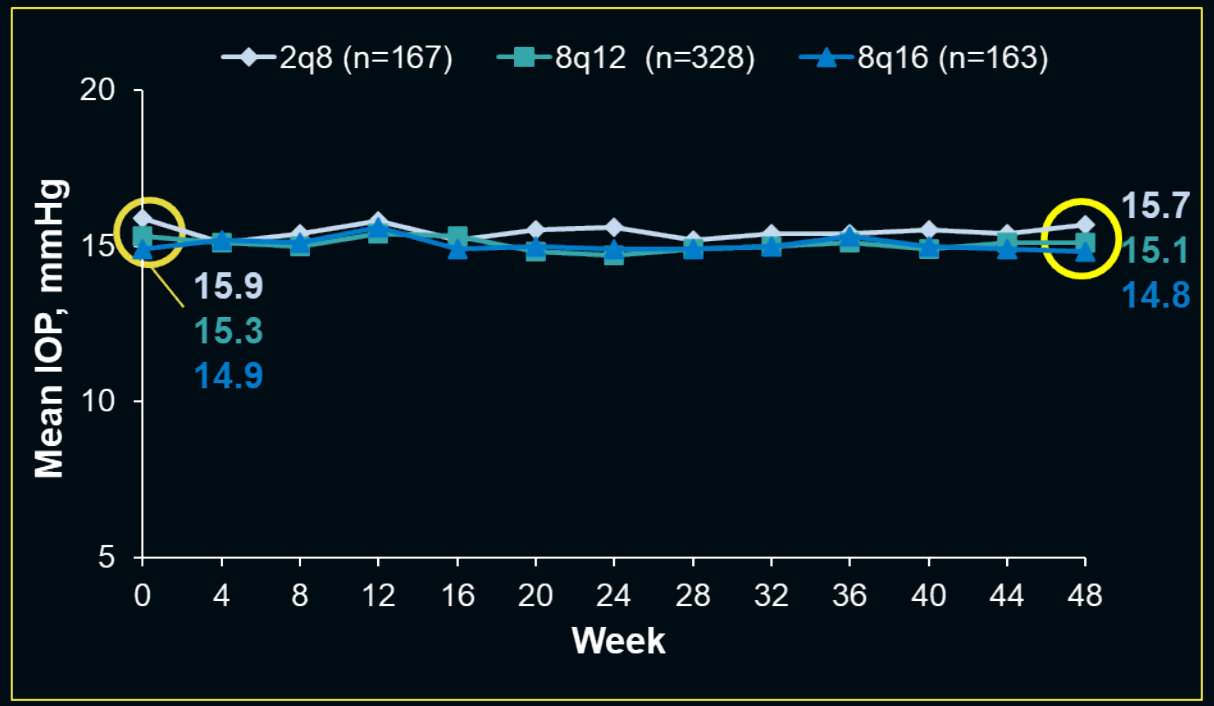
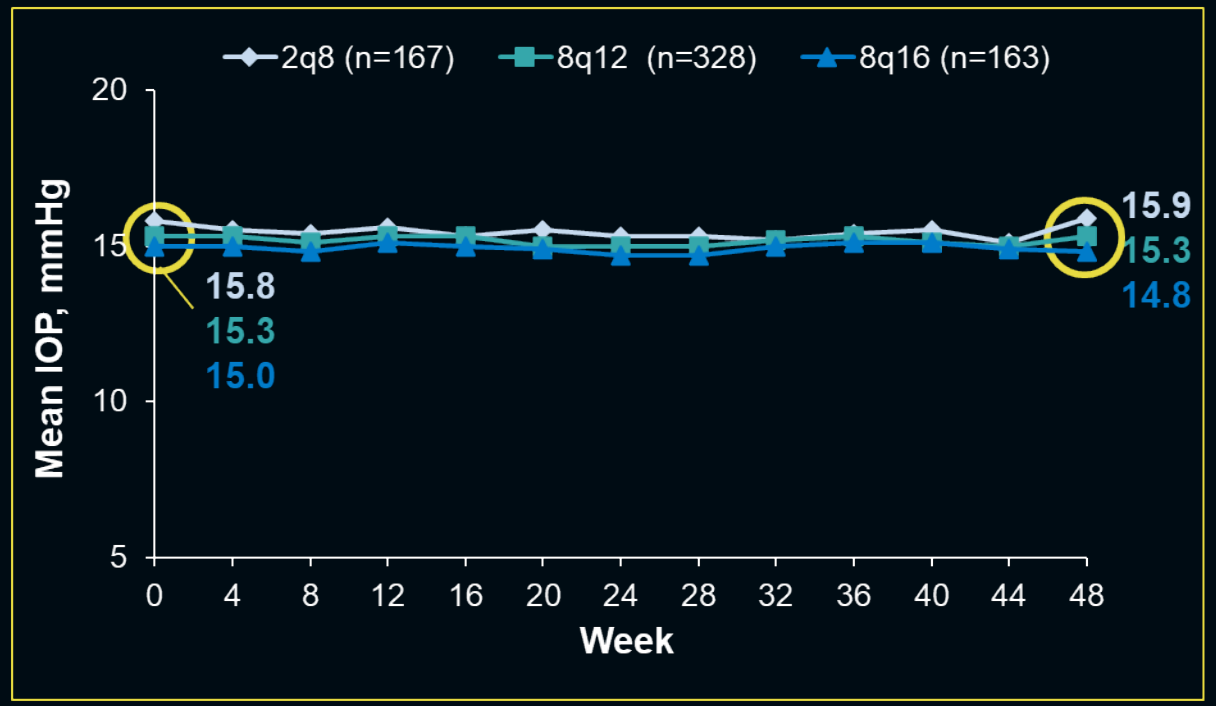
Study Eye



Fellow Eye (Treated and Untreated)



Through Week 48, 62% of fellow eyes received aflibercept 2 mg at the discretion of the study investigator

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

Mean Pre-dose IOP Values in Study and Untreated Fellow Eyes Were Similar Through Week 48

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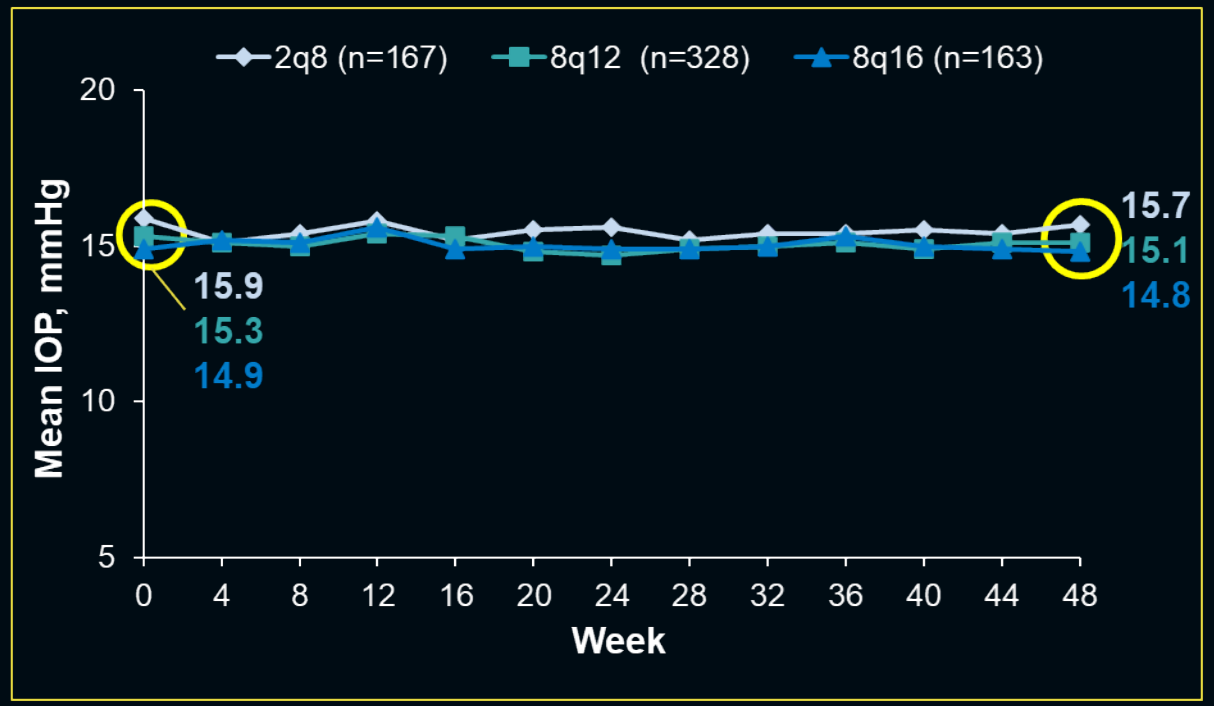
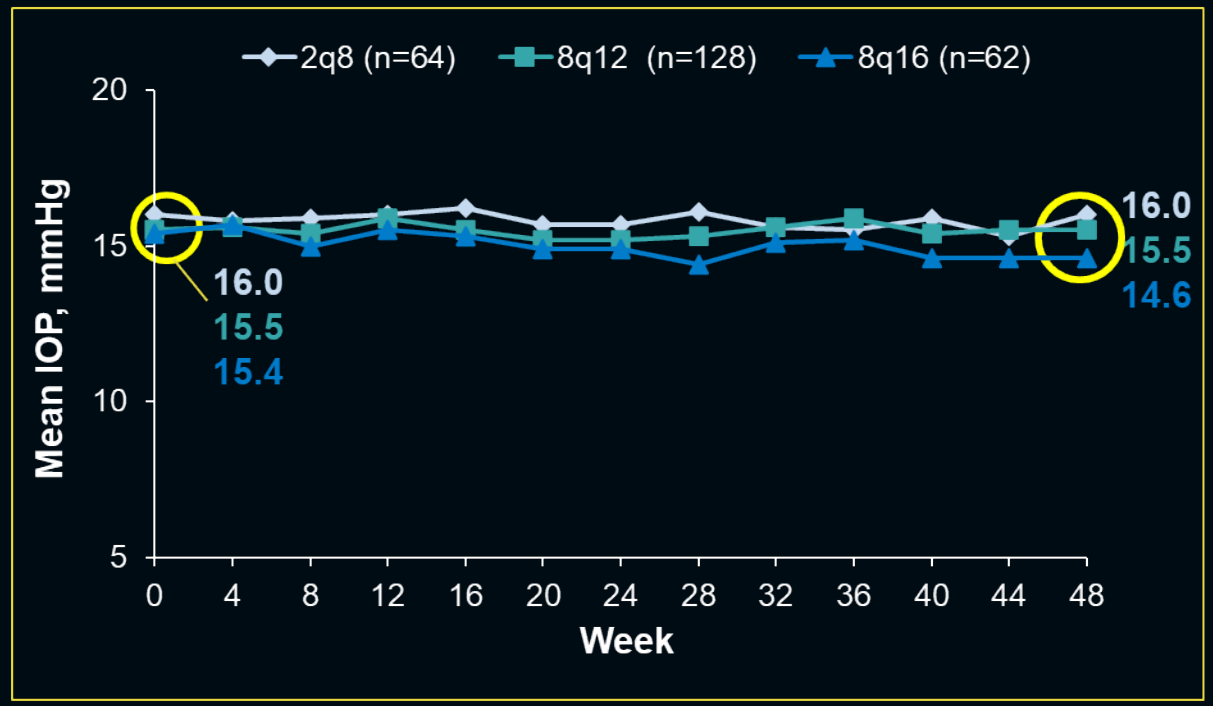
Study Eye



Fellow Eye (Untreated)



Safety analysis set.

Change in Pre-dose IOP Values in Study and Fellow Eyes Were Similar Through Week 48

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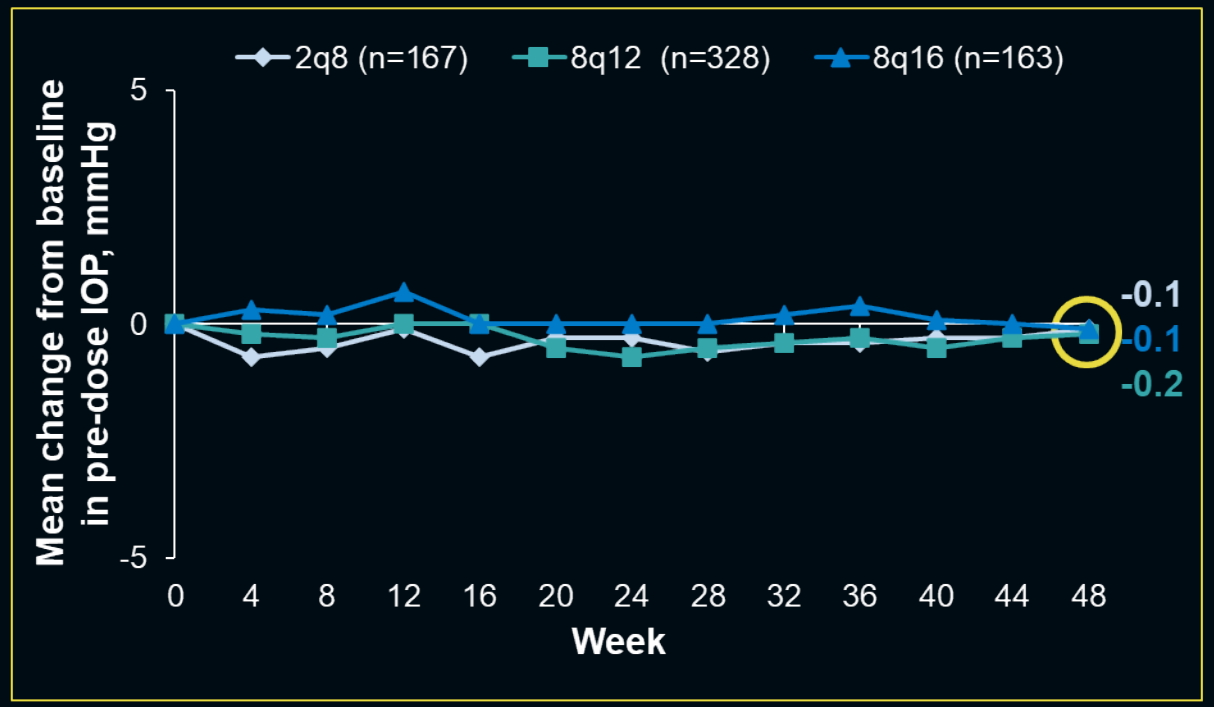
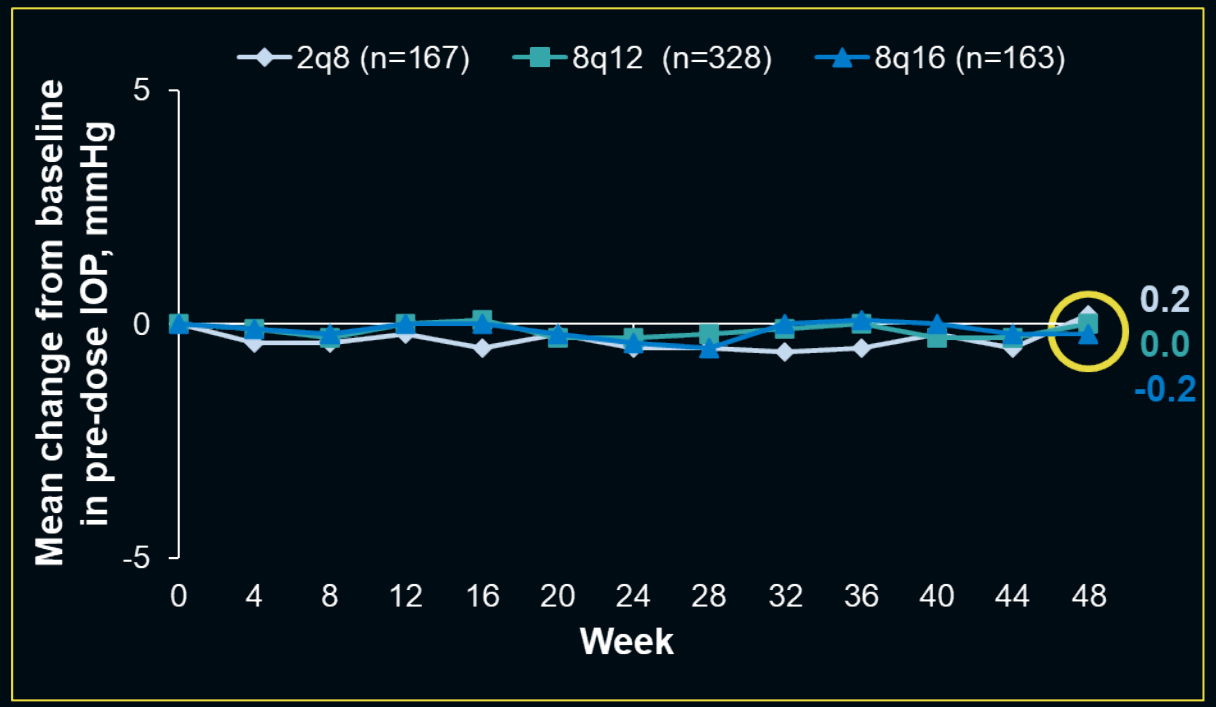
Study Eye



Fellow Eye (Treated[a] and Untreated)



Through Week 48, 62% of fellow eyes received aflibercept 2 mg at the discretion of the study investigator

Safety analysis set.
[a]Through Week 48, fellow eye injections with aflibercept 2 mg were reported in 61.7%, 61.0%, and 62.0% of patients in the 2q8, 8q12, and 8q16 groups, respectively.
Study eyes in 2q8, 8q12, and 8q16, received a mean of 7.7, 5.7, and 4.9 injections, respectively, through Week 48.
Fellow eyes in 2q8, 8q12, and 8q16, received a mean of 6.4, 5.8, and 6.5 injections, respectively, through Week 48.

Change in Pre-dose IOP Values in Study and Untreated Fellow Eyes Were Similar Through Week 48

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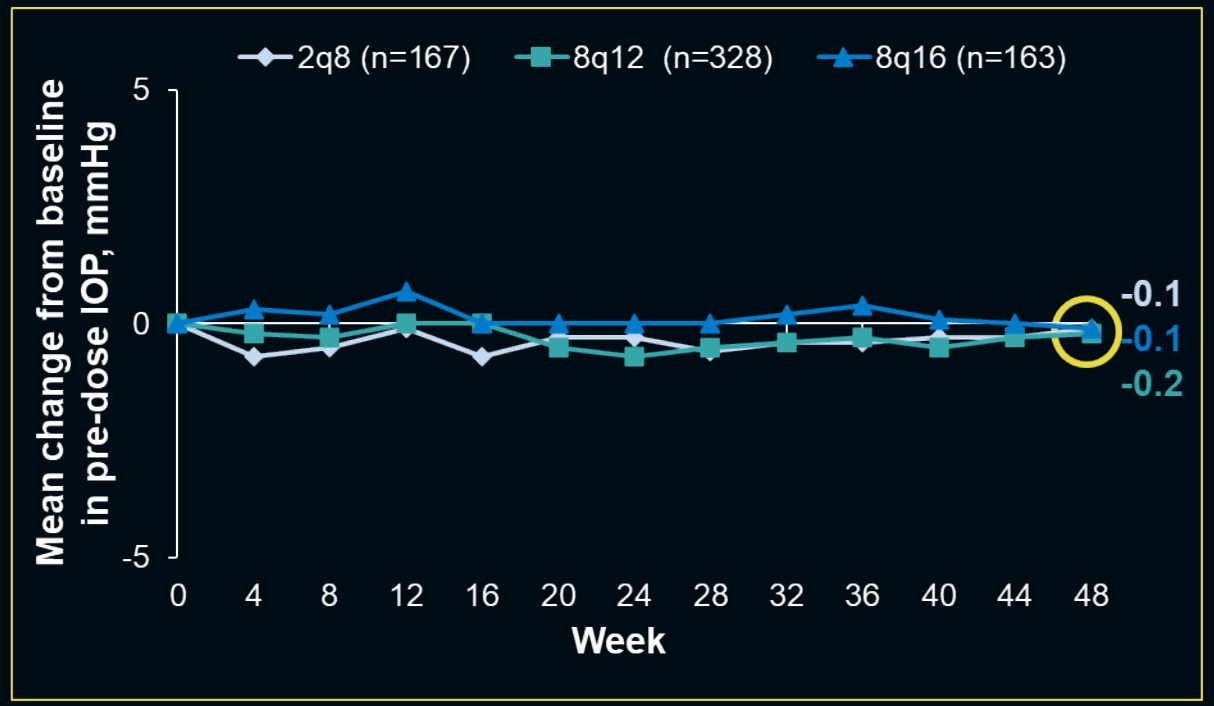
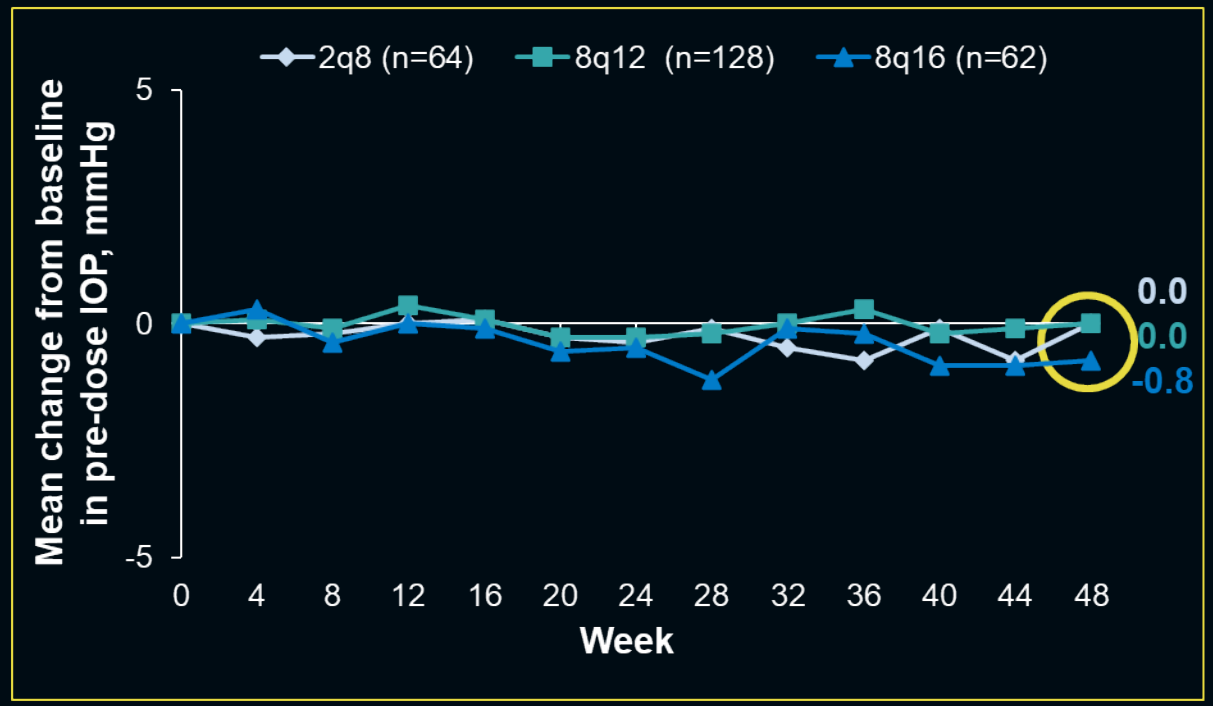
DME

Study Eye



Fellow Eye (Untreated)



Safety analysis set.

Cumulative Incidence of Eyes Meeting Pre-dose IOP Analysis Criteria Through Week 48

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	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%	0.6%[c]	0.0%
Pre-dose IOP ≥30 mmHg at any visit	0.0%	0.3%[b]	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 ocular hypertension in the fellow eye.

[c]History of glaucoma or ocular hypertension.

IOP Through Week 48 in the Study Eye

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	2q8 (n=167)	8q12 (n=328)	8q16 (n=163)	All 8 mg (n=491)
IOP ≥35 mmHg pre- or post-injection at any visit, n (%)	2 (1.2)	1 (0.3)	0 (0.0)	1 (0.2)

Safety analysis set.

Mean Change in Pre-dose to Post-dose IOP in Study Eyes at Active Dosing Visits

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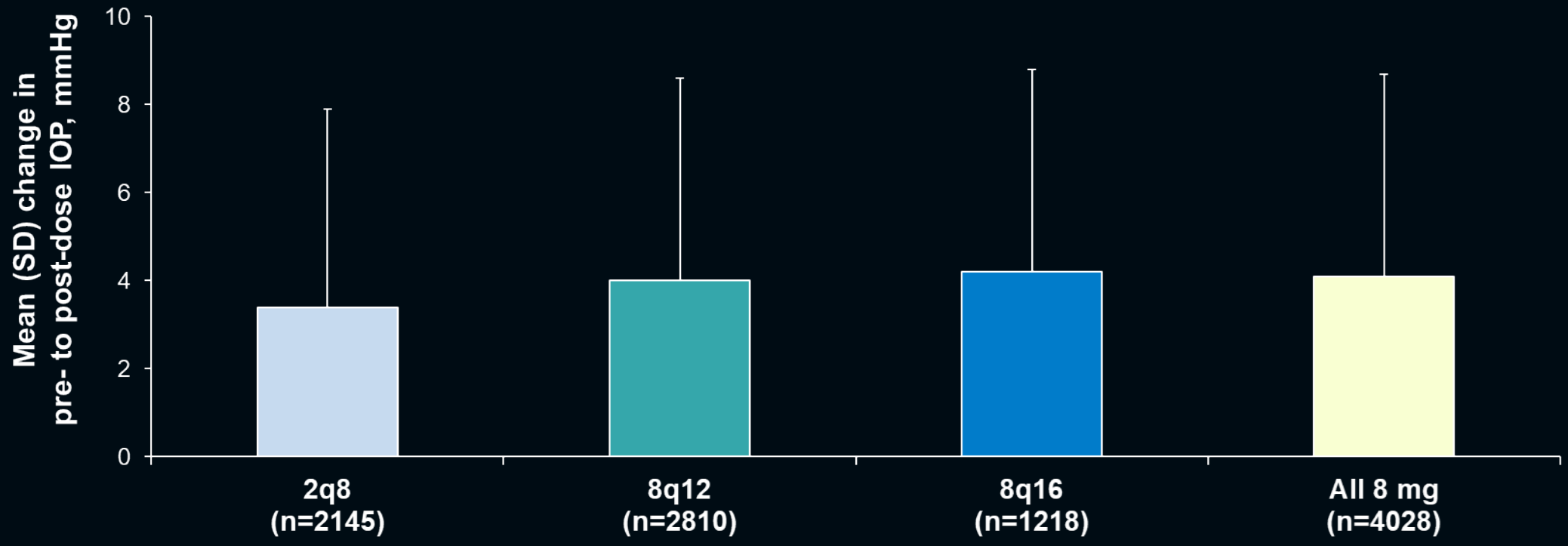

Mean change from pre- to post-dose IOP was similar across treatment groups

Safety analysis set: 2q8 n=167; 8q12 n=328; 8q16 n= 163; All 8 mg n=491.
n=number of visits.

IOP-lowering Medications in Eyes Without Glaucoma-related History Through Week 48

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	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 no glaucoma-related history, 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 (%)	3 (1.9)	4 (1.3)	1 (0.7)	2 (1.3)	3 (1.0)	0 (0.0)

The proportions of study and fellow eyes **without glaucoma-related history requiring an IOP-lowering agent** were low and comparable across treatment groups

Safety analysis set.
[a]Treated and untreated fellow eyes. [b]No medical history of glaucoma/glaucoma suspect and not receiving 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; IOP-lowering agents: beta blocking agents, prostaglandin analogues, carbonic anhydrase inhibitors, or other anti-glaucoma preparations.

IOP-lowering Medications in Eyes Without Glaucoma-related History Through Week 48

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	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 no glaucoma-related history, 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 (%)	**3 (1.9)**	4 (1.3)	1 (0.7)	**2 (1.3)**	3 (1.0)	0 (0.0)

3 unique patients (5 eyes) started an IOP-lowering agent:
- 2 patients were treated OU
- 1 patient was treated in the study eye only

Safety analysis set.
OU, both eyes.
[a]Treated and untreated fellow eyes. [b]No medical history of glaucoma/glaucoma suspect and not receiving 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; IOP-lowering agents: beta blocking agents, prostaglandin analogues, carbonic anhydrase inhibitors, or other anti-glaucoma preparations.

IOP-lowering Medications in Eyes Without Glaucoma-related History Through Week 48

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DME

	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 no glaucoma-related history, 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 (%)	3 (1.9)	**4 (1.3)**	1 (0.7)	2 (1.3)	**3 (1.0)**	0 (0.0)

4 unique patients (7 eyes) started an IOP-lowering agent:

- 3 patients were treated OU
- 1 patient was treated in the study eye only

Safety analysis set.
OU, both eyes.
[a]Treated and untreated fellow eyes. [b]No medical history of glaucoma/glaucoma suspect and not receiving 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; IOP-lowering agents: beta blocking agents, prostaglandin analogues, carbonic anhydrase inhibitors, or other anti-glaucoma preparations.

IOP-lowering Procedures[a] in All Patients Through Week 48

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	Study Eye			Fellow Eye[a]		
	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[b] through Week 48, n (%)	0 (0.0)	2 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)

- Anterior chamber paracentesis was the only IOP-lowering procedure reported through Week 48[c]

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

Conclusions

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- In patients with DME, pre-dose IOP values in the study eye were similar through Week 48 across treatment groups
- Pre-dose IOP values were similar through Week 48 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)