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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Disclosures

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- Dr. Grewal is a consultant for Apellis, Priovant, Zeiss, Astellas, Regeneron Pharmaceuticals, Inc., and Roche
- The PHOTON study was sponsored by Regeneron Pharmaceuticals, Inc. (Tarrytown, New York) and co-funded by Bayer AG (Leverkusen, Germany). This analysis was funded by Regeneron Pharmaceuticals, Inc. (Tarrytown, New York). The sponsors participated in the design and conduct of this analysis, interpretation of the data, and preparation of this presentation
- Study disclosures: This study includes research conducted on human patients. Institutional review board approval was obtained prior to study initiation
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Background

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- 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 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

DME, diabetic macular edema; IOP, intraocular pressure.

PHOTON Study Design

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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 patients with DME.
2q8, 2 mg every 8 weeks; 8q12, 8 mg every 12 weeks; 8q16, 8 mg every 16 weeks; BCVA, best-corrected visual acuity.

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 the 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 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

[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 96

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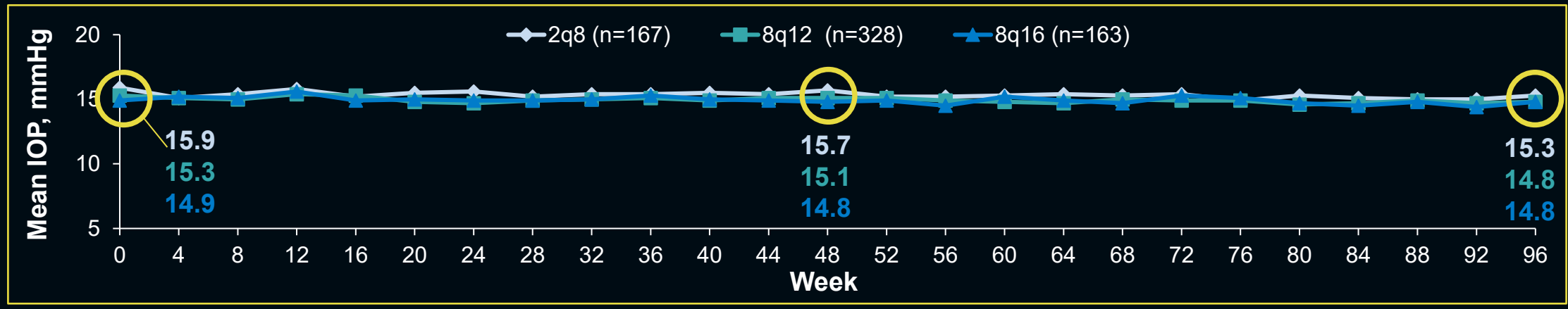
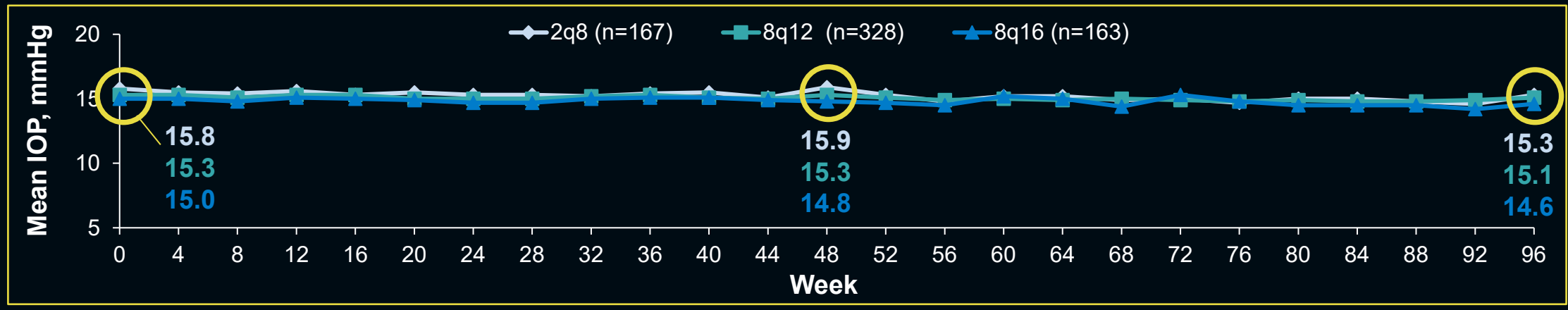
Study Eye



Fellow Eye (2-mg Treated and Untreated)



Through Week 96, ~70% 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 14.0, 9.0, and 8.0 injections, respectively, through Week 96.
Fellow eyes in 2q8, 8q12, and 8q16, received a mean of 10.0, 9.4, and 10.8 injections, respectively, through Week 96.

Mean Change in Pre-Dose IOP Values in Study and Fellow Eyes Were Similar Through Week 96

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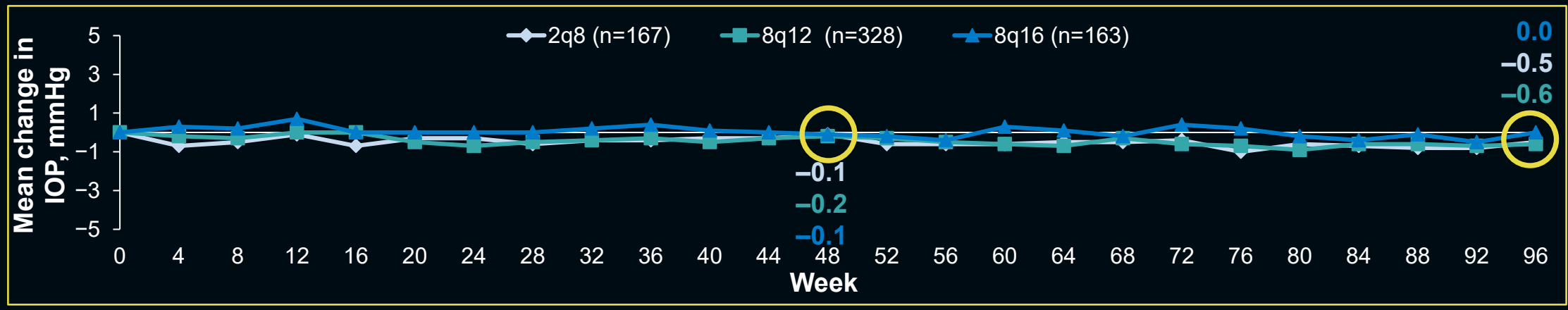
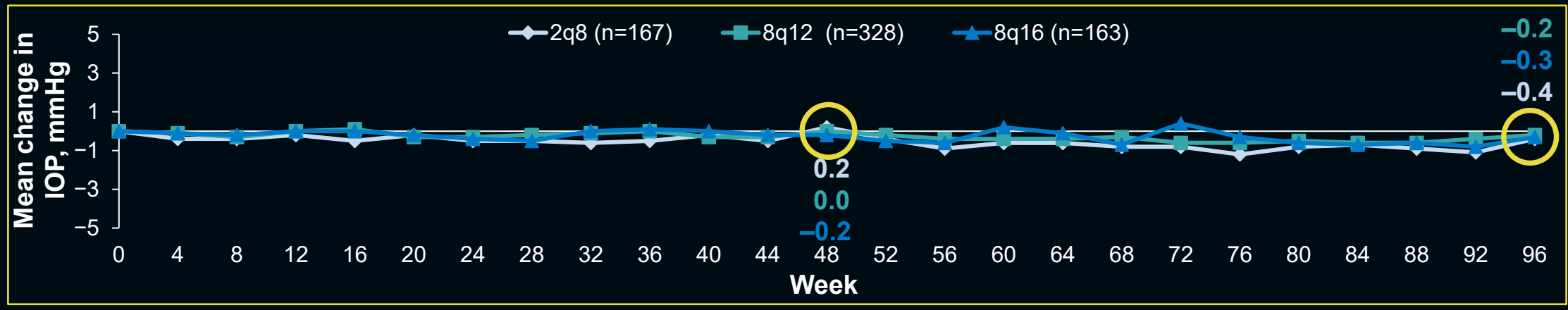
Study Eye



Fellow Eye (2-mg Treated and Untreated)



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Fellow eyes in 2q8, 8q12, and 8q16, received a mean of 10.0, 9.4, and 10.8 injections, respectively, through Week 96.

Mean Pre-Dose IOP Values in Study and Untreated Fellow Eyes Were Similar Through Week 96

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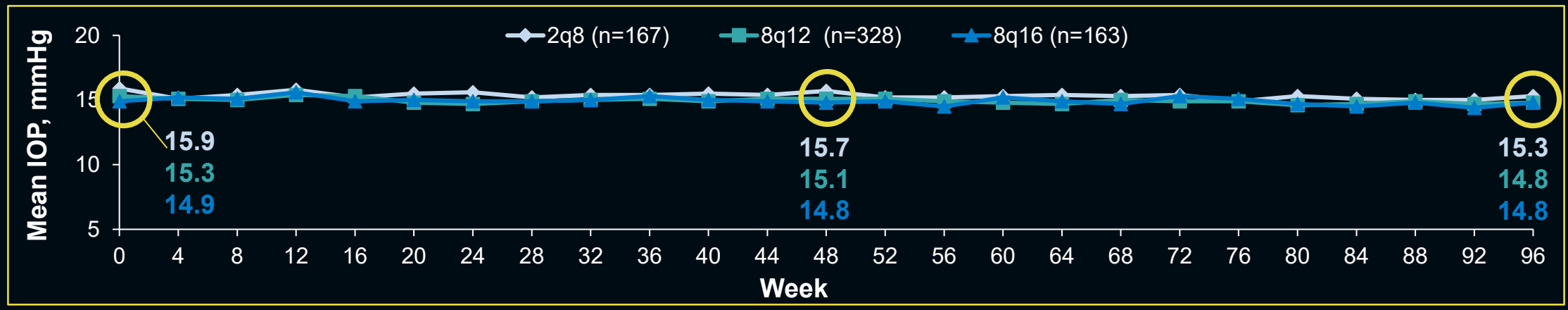
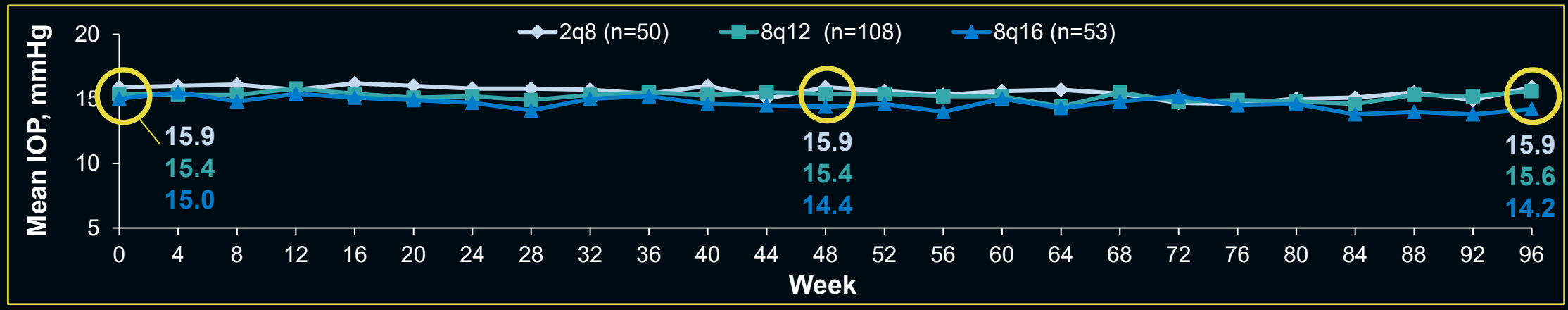
Study Eye



Fellow Eye (Untreated)



Through Week 96, ~70% 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 14.0, 9.0, and 8.0 injections, respectively, through Week 96.

Mean Change in Pre-Dose IOP Values in Study and Untreated Fellow Eyes Were Similar Through Week 96

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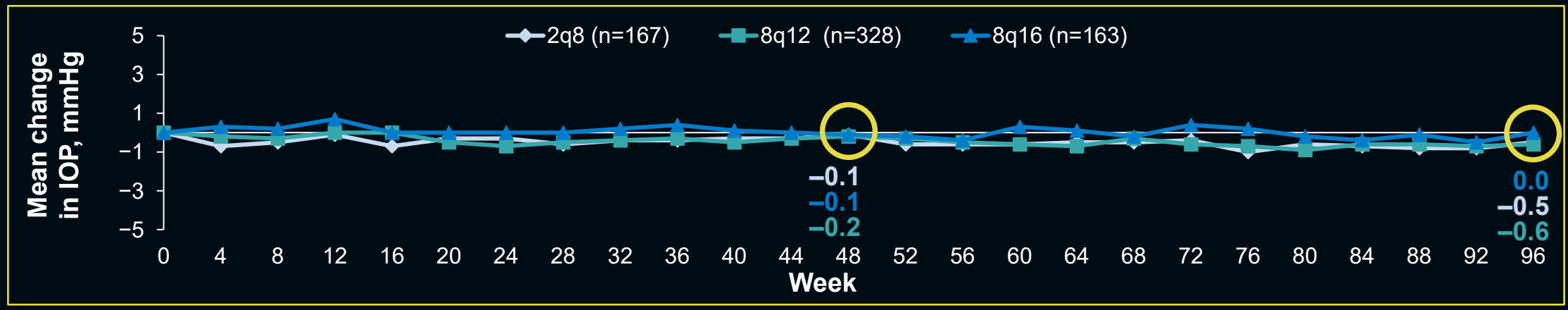
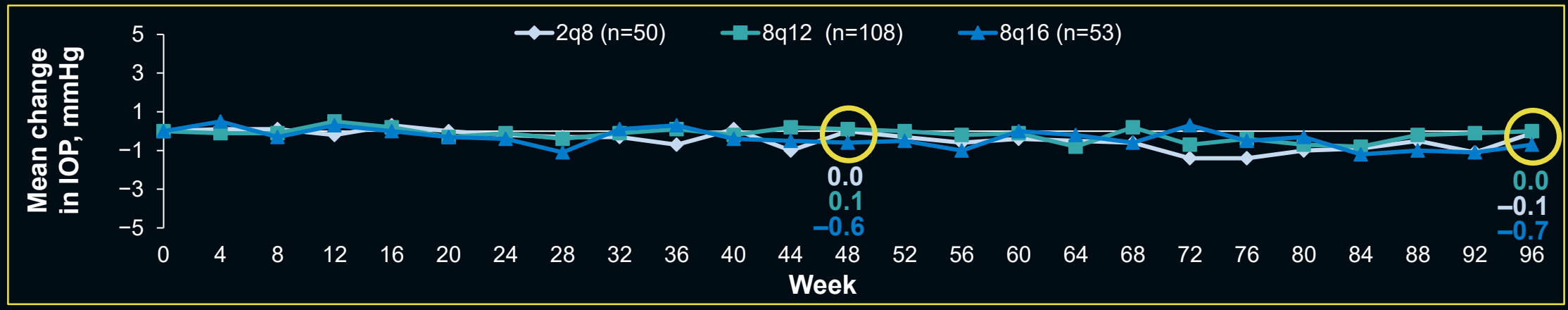
Study Eye



Fellow Eye (Untreated)



Through Week 96, ~70% 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 an average of 14.0, 9.0, and 8.0 injections, respectively, through Week 96.

Cumulative Incidence of Patients Meeting IOP Criteria Through Week 96

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	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 combined.

IOP Through Week 96 in Study and Fellow Eyes

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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)
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, all study eye randomization arms combined.

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)
Glaucoma-related history:						
Eyes with a medical history of glaucoma/ glaucoma suspect[b]	13 (7.8)	26 (7.9)	13 (8.0)	13 (7.8)	33 (10.1)	16 (9.8)
AND/OR						
Receiving ≥1 IOP-lowering agent[c] at baseline, n (%)						

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

Safety analysis set.
[a]2-mg treated and untreated fellow eyes, all study eye randomization arms combined.
[b]Medical history of glaucoma/glaucoma suspect and/or 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, IOP increased.
[c]IOP-lowering agents: beta blocking agents, prostaglandin analogues, carbonic anhydrase inhibitors, or other antiglaucoma preparations; there was 1 patient on an IOP-lowering agent at baseline without a recorded history of glaucoma/glaucoma suspect.

IOP-Lowering Medications in Eyes Without Glaucoma-Related History Through Week 96

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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]	154 (92.2)	302 (92.1)	150 (92.0)	154 (92.2)	295 (90.0)	147 (90.2)
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)

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

Safety analysis set.

[a]2-mg treated and untreated fellow eyes, all study eye randomization arms combined.

[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 antiglaucoma preparations.

IOP-Lowering Medications in Eyes With Glaucoma-Related History Through Week 96

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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 glaucoma-related history, n (%)[b]	13 (7.8)	26 (7.9)	13 (8.0)	13 (7.8)	33 (10.1)	16 (9.8)
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)

The proportions of study and fellow eyes **with glaucoma-related history requiring a new IOP-lowering agent** were low and comparable across treatment groups

Safety analysis set.
[a]2-mg treated and untreated fellow eyes, all study eye randomization arms combined.
[b]Medical history of glaucoma/glaucoma suspect and/or 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, IOP increased; IOP-lowering agents: beta blocking agents, prostaglandin analogues, carbonic anhydrase inhibitors, or other antiglaucoma preparations.

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

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DME

	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, all study eye randomization arms combined.

Conclusions

- 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)
- 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 96
- Only 4 study eyes receiving aflibercept 8 mg and 2 fellow eyes required anterior chamber paracentesis through Week 96

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)