The 16th Congress of the
ASIA-PACIFIC VITREO-RETINA SOCIETY
held in conjunction with APOIS 2023 Congress, APSEG 2023 Annual Meeting and ASMHK 2023
December 8-10, 2023 | Hong Kong Convention and Exhibition Centre
APVRS 2023 HONG KONG
Hosts

Aflibercept 8 mg for Diabetic Macular Edema: 96-Week Results From the Phase 2/3 PHOTON Trial

Abstract No: 200504

Andrew Chang,[1] Diana V. Do,[2] on behalf of the PHOTON study investigators
[1]Sydney Retina, Sydney, New South Wales, Australia; [2]Byers Eye Institute, Stanford University School of Medicine, Palo Alto, CA, USA

PURPOSE

To evaluate the efficacy and safety of intravitreal aflibercept injection 8 mg versus 2 mg in patients with treatment-naïve or previously treated diabetic macular edema (DME).

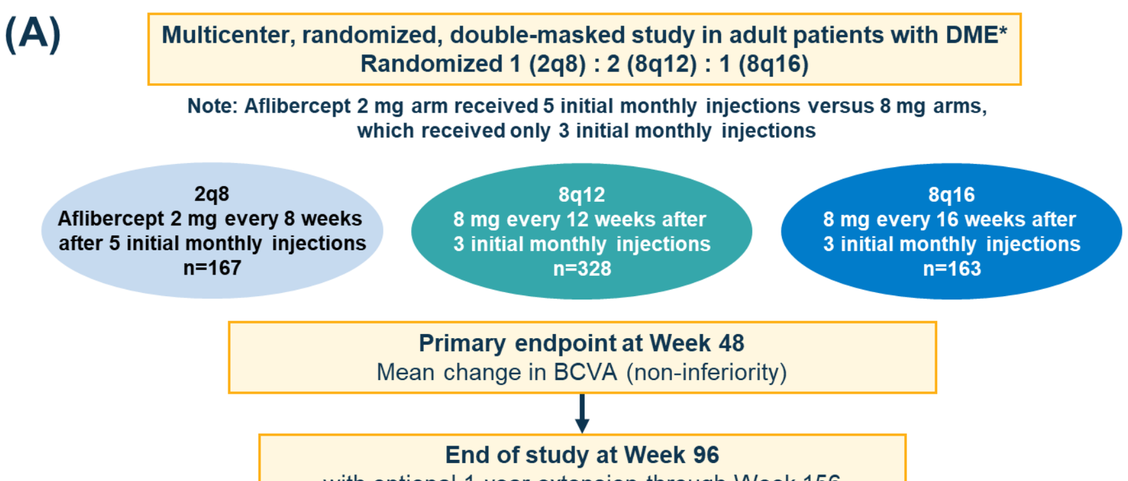
METHODS

PHOTON (NCT04429503) was a 96-week, Phase 2/3, double-masked, non-inferiority trial in which patients with DME were randomized to receive aflibercept 8 mg (70 µL injection), every 12 or 16 weeks after three monthly doses or aflibercept 2 mg (50 µL injection) every 8 weeks after five monthly doses (**Figure 1A**). The dosing interval for patients in the 8q12 and 8q16 groups could be shortened from Week 16 and extended from Week 52 based on protocol criteria (**Figure 1B**).

Exploratory endpoints included mean change in BCVA at Week 96 and the proportion of patients with ≥12- and ≥16-week dosing intervals through Week 96.

FIGURE 1: (A) PHOTON Study Design and (B) Dosing Schedule with Dose Regimen Modification

(A)



(B)

YEAR 1	Day 1	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32	Week 36	Week 40	Week 44	Week 48 (Primary Endpoint)
2q8	X	X	X	X	X	o	X	o	X	o	X	o	X
8q12	X	X	X	o	o[a]	X[a]	o	o	X[a]	o	o	X[a]	o
8q16	X	X	X	o	o[a]	o[a]	X[a]	o	o	o	X[a]	o	o

YEAR 2	Week 52	Week 56	Week 60	Week 64	Week 68	Week 72	Week 76	Week 80	Week 84	Week 88	Week 92	Week 96
2q8	o	X	o	X	o	X	o	X	o	X	o	o
8q12	o	X[a, b]	o	o	X[a, b]	o	o	X[a, b]	o	o	X[a, b]	o
8q16	o	X[a, b]	o	o	o	X[a, b]	o	o	o	X[a, b]	o	o

[a]DRM: Interval Shortening During Years 1 and 2

- **Criteria for interval shortening:**
  - >10-letter loss in BCVA from Week 12 due to persistent or worsening DME **AND**
  - >50-µm increase in CST from Week 12
- Patients who met DRM criteria had dosing intervals shortened to Q8 at **Weeks 16** and **20** or by 4-week increments from **Week 24**
  - The minimum interval was **Q8**

[b]DRM: Interval Extension During Year 2

- **Criteria for interval extension:**
  - <5-letter loss in BCVA from Week 12 **AND**
  - CST <300 µm (or <320 µm on Spectralis)
- Patients who met DRM criteria beginning at **Week 52** had dosing intervals extended by 4-week increments
  - The maximum assigned interval was **Q24**

Stippled boxes=initial treatment phase; X=active injection; o=sham injections. Figure does not reflect all dosing options once a patient's interval is shortened or extended. *Treatment naïve and previously treated patients aged ≥18 years with type 1 or type 2 diabetes, DME with central involvement with CST ≥300 µm in the study eye, and BCVA of 78-24 letters (Snellen equivalent of 20/32-20/320) with decreased vision due to DME. BCVA, best corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; DRM, dose regimen modification. Q8, every 8 weeks; Q24, every 24 weeks.

RESULTS

Overall, 658 patients (8q12: n=328; 8q16: n=163; 2q8: n=167) were enrolled (mean±SD age, 62.3±10.4 years; 39.1% female), and 80.9% completed the study at Week 96 (**Table 1**).

TABLE 1: Baseline Demographics and Characteristics

	2q8	8q12	8q16	Total
N (FAS/SAF)	167	328	163	658
Completion rate at Week 48 (%)	94.0	91.2	95.1	92.9
Completion rate at Week 96 (%)	83.2	77.8	84.8	80.9
Age (years)	63.0 (9.8)	62.1 (11.1)	61.9 (9.5)	62.3 (10.4)
Female (%)	44.9	36.0	39.3	39.1
Race (%)				
White	67.1	70.4	78.5	71.6
Asian	18.0	14.6	14.1	15.3
Black or African American	10.8	10.7	5.5	9.4
Other*	2.4	3.0	0.6	2.4
Not reported	1.8	1.2	1.2	1.4
Ethnicity (%)				
Hispanic or Latino	18.6	16.5	20.9	18.1
Duration of diabetes (years)	15.9 (10.0)	15.1 (10.0)	15.7 (10.7)	15.5 (10.2)
Hemoglobin A_{1c} (%)	8.1 (1.5)	7.9 (1.5)	7.8 (1.5)	8.0 (1.5)
BMI (kg/m²)	29.9 (6.5)	30.4 (6.2)	31.0 (6.1)	30.5 (6.2)
BCVA (ETDRS letters)	61.5 (11.2)	63.6 (10.1)	61.4 (11.8)	62.5 (10.9)
CST (µm)	457.2 (144.0)	449.1 (127.4)	460.3 (117.8)	454.0 (129.5)
Prior treatment for DME (%)	44.3	43.6	43.6	43.8

Data are mean (SD) unless otherwise indicated. FAS: all randomized patients who received ≥1 study treatment. SAF: all patients who received study treatment. *Other includes patients who were American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and multiracial. BCVA, best corrected visual acuity; BMI, body mass index; CST, central subfield thickness; DME, diabetic macular edema; ETDRS, Early Treatment of Diabetic Retinopathy Study; FAS, full analysis set; SAF, safety analysis set.

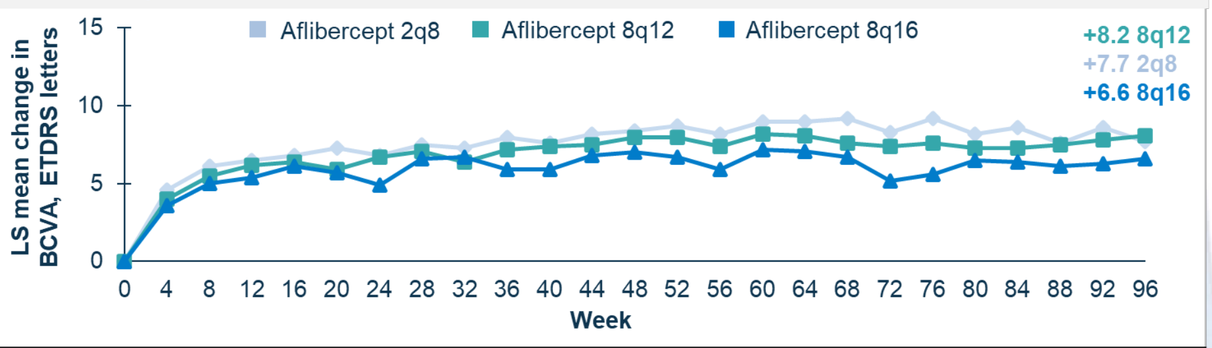
RESULTS (cont.)

Mean BCVA change from baseline at Week 96 was +7.7 (2q8), +8.2 (8q12), and +6.6 (8q16) letters (least squares mean difference: non-inferiority at 4-letter margin 8q12 vs 2q8: [nominal P<0.0001]; 8q16 vs 2q8: [nominal P=0.0044]) (**Figure 2**).

Through Week 96, 88% (8q12) and 84% (8q16) of patients maintained ≥12- and ≥16-week dosing intervals, respectively (**Figure 3**).

Safety outcomes for aflibercept 8 mg and 2 mg were similar through Week 96 (**Table 2**). Ocular AEs occurring in ≥5% of patients in any treatment group were cataract, vitreous floaters, and conjunctival hemorrhage. No cases of ischemic optic neuropathy or occlusive retinal vasculitis were reported through Week 96 in any treatment arm. No clinically relevant change in intraocular pressure was observed in any treatment arm.

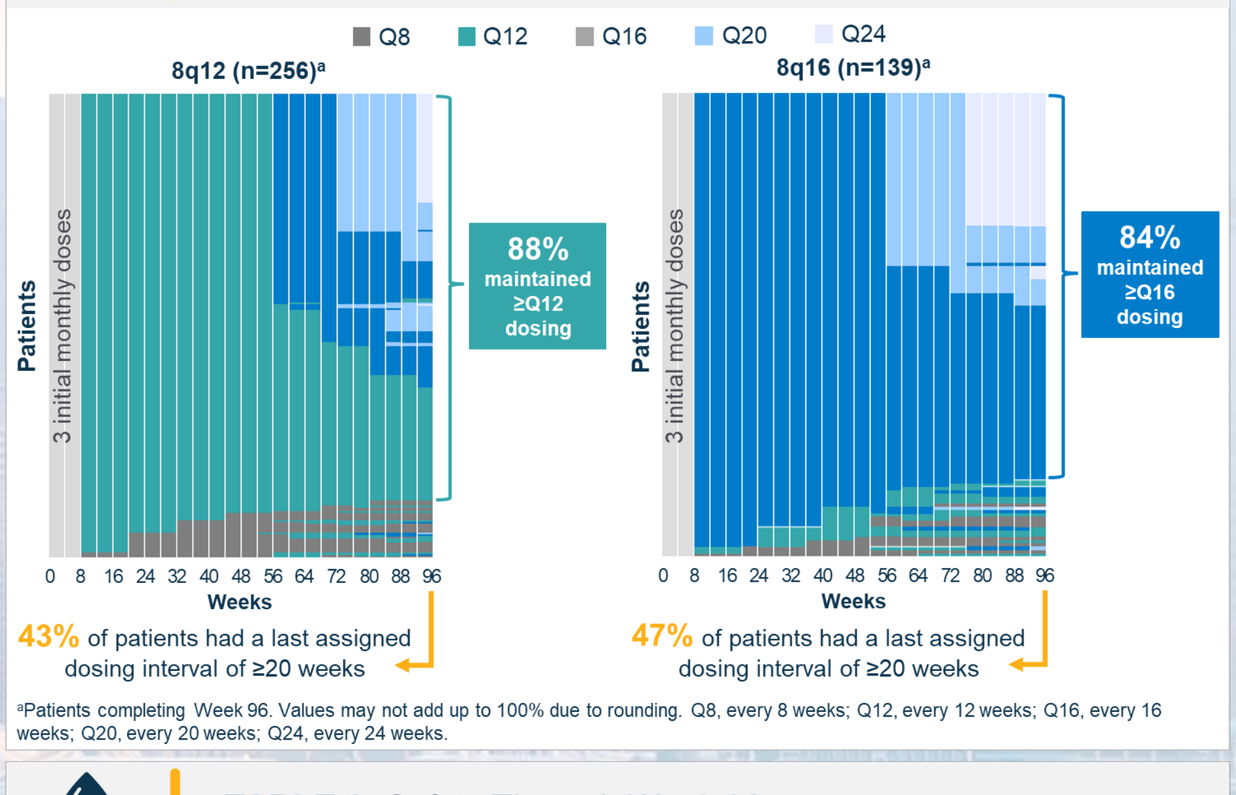
FIGURE 2: Mean Change in BCVA From Baseline Through Week 96



	Mean number of injections[a]	LS mean change from BL at **Week 96** (MMRM)	Diff. in LS means vs. 2q8	2-sided 95% CI	1-sided test for non-inferiority at 4-letter margin
2q8	13.8	7.7			
8q12	9.5	8.2	+0.45	-1.55, 2.45	p < 0.0001 (nominal)
8q16	7.8	6.6	-1.11	-3.27, 1.05	p = 0.0044 (nominal)

Data shown in the figure represent LS mean values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at baseline). LS mean values were generated using MMRM, with baseline BCVA as a covariate, treatment group (aflibercept 2q8, 8q12, 8q16) and stratification variables (geographic region [Japan vs rest of the world], baseline CST [<400 µm vs ≥400 µm], prior treatment for DME [yes vs no]) as fixed factors, and interaction terms for baseline and visit and for treatment and visit. [a]Patients completing Week 96: 2q8 n=139; 8q12 n=256; 8q16 n=139. BCVA, best corrected visual acuity; BL, baseline; ETDRS, Early Treatment of Diabetic Retinopathy Study; ICE, intercurrent event; LS, least squares; MMRM, mixed model for repeated measures.

FIGURE 3: Proportion of Patients Who Maintained or Extended Intervals Through Week 96



[a]Patients completing Week 96. Values may not add up to 100% due to rounding. Q8, every 8 weeks; Q12, every 12 weeks; Q16, every 16 weeks; Q20, every 20 weeks; Q24, every 24 weeks.

TABLE 2: Safety Through Week 96

	2q8	8q12	8q16	All 8 mg
N (SAF)	167	328	163	491
Ocular safety				
Patients with ≥1 ocular AE (%)[a]	37.1	43.9	45.4	44.4
Patients with ≥1 IOI AE (%)[a]	1.2	1.5	0.6	1.2
Patients with IOP ≥35 mmHg pre- or post-injection (%)[b]	1.2	0.6	0	0.4
Non-ocular safety				
APTC events (%)[a]	7.2	6.7	6.7	6.7
Hypertension events (%)[a]	16.2	15.5	20.9	17.3
Non-ocular SAEs (%)[a]	25.1	22.9	23.9	23.2
Deaths (%)[c]	5.4	5.5	3.1	4.7

[a]Treatment-emergent. [b]IOP was measured in the study eye. [c]All events. AE, adverse event; APTC, Anti-Platelet Trialists' Collaboration; IOI, intraocular inflammation; IOP, intraocular pressure; SAE, serious adverse event; SAF, safety analysis set.

CONCLUSIONS

- 8q12 and 8q16 groups achieved similar BCVA gains compared to 2q8 at Week 96, with an average of 4.3 and 6 fewer injections, respectively
- Through Week 96, 88% of 8q12 patients and 84% of 8q16 patients maintained ≥12- and ≥16-week dosing intervals, respectively
  - At Week 96, 43% of 8q12 patients and 47% of 8q16 patients had a last assigned dosing interval of ≥20 weeks
- Safety of aflibercept 8 mg was comparable to that of aflibercept 2 mg over 96 weeks

Disclosures: Dr Chang has received consulting fees from Alcon, Allergan, Bayer, Novartis, and Roche. 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.
Funding: This study was sponsored by Regeneron Pharmaceuticals, Inc. (Tarrytown, NY, USA) and co-funded by Bayer AG (Leverkusen, Germany). The sponsor participated in the design and conduct of the study, analysis of the data, and preparation of this abstract. Medical writing support for this encore, under the direction of the authors, was provided by ApotheCom and funded by Bayer Consumer Care AG, Basel, Switzerland, in accordance with Good Publication Practice (GPP) guidelines (Ann Intern Med 2022;175:1298–1304).
Study disclosures: This study includes research conducted on human patients. Institutional Review Board approval was obtained prior to study initiation. These data were previously presented at the American Academy of Ophthalmology 2023 Meeting, November 3–6, 2023.

Presented at the Asia-Pacific Vitreo-Retina Society Congress, December 8–10, 2023.