Baseline Characteristics and Outcomes of Patients Treated With Aflibercept 8 mg at Shortened Dosing Intervals in PHOTON

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Background

- Aflibercept 8 mg is a novel formulation that delivers a 4-fold higher molar dose than aflibercept 2 mg, potentially suppressing VEGF signaling over a longer duration
- In the PHOTON trial, aflibercept 8 mg demonstrated non-inferior BCVA gains with extended dosing intervals versus aflibercept 2 mg in patients with DME, with no new safety signals through Week 96[1,2]
- PHOTON allowed for dose regimen modification for aflibercept 8 mg, based on responses to treatment
- It is important to characterize patients with DME who required a different dosing regimen with aflibercept 8 mg to inform optimal treatment strategy

This analysis evaluated baseline characteristics and visual and anatomic outcomes of patients with DME who had their dosing interval shortened, maintained or extended through Week 96 in the PHOTON trial

BCVA, best-corrected visual acuity; DME, diabetic macular edema; VEGF, vascular endothelial growth factor.
1. Brown DM et al. *Lancet*. 2024;403:1153–1163. 2. Do D. Presented at: Angiogenesis, Exudation, and Degeneration; February 3, 2024; Virtual Meeting.

PHOTON Study Design

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

Note: 2-mg arm received 5 initial monthly injections versus 8-mg arms, which received only 3 initial monthly injections

2q8
Aflibercept 2 mg every 8 weeks after 5 initial monthly injections
n=167

8q12
8 mg every 12 weeks after 3 initial monthly injections
n=328

8q16
8 mg every 16 weeks after 3 initial monthly injections
n=163

Primary endpoint at Week 48
Mean change in BCVA (noninferiority)

↓

End of study at Week 96
with optional 1-year extension through Week 156

[a]Treatment-naive and previously treated patients aged ≥18 years with type 1 or type 2 diabetes, DME with central involvement with CRT ≥300 µm in the study eye, and BCVA of 78-24 ETDRS letters (Snellen equivalent of 20/32-20/320) with decreased vision due to DME.
2q8, 2 mg every 8 weeks; 8q12, 8 mg every 12 weeks; 8q16, 8 mg every 16 weeks; CRT, central retinal thickness; ETDRS, Early Treatment Diabetic Retinopathy Study.

PHOTON: Dosing Schedule and Dose Regimen Modification

Primary Endpoint

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
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	-
8q12	o	X[a,b]	o	o	X[a,b]	o	o	X[a,b]	o	o	X[a,b]	-
8q16	o	X[a,b]	o	o	o	X[a,b]	o	o	o	X[a,b]	o	-

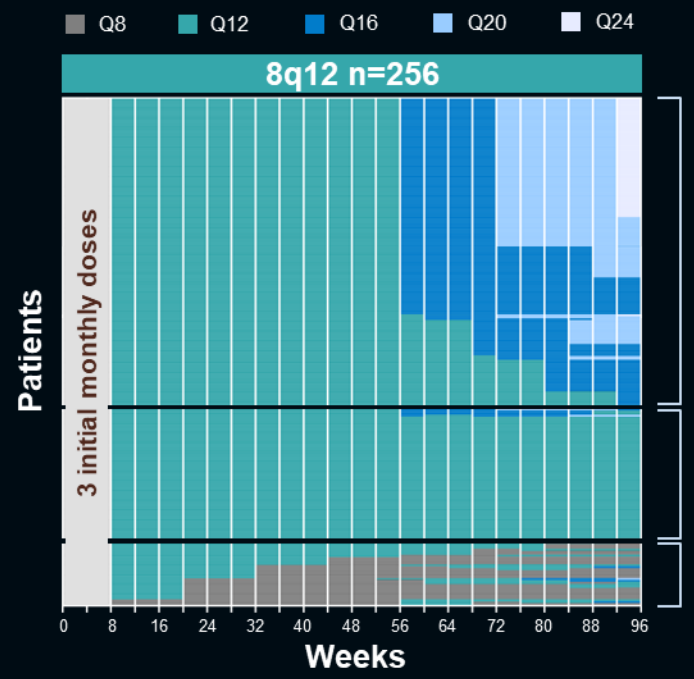
[a]DRM: Interval Shortening During Years 1 and 2

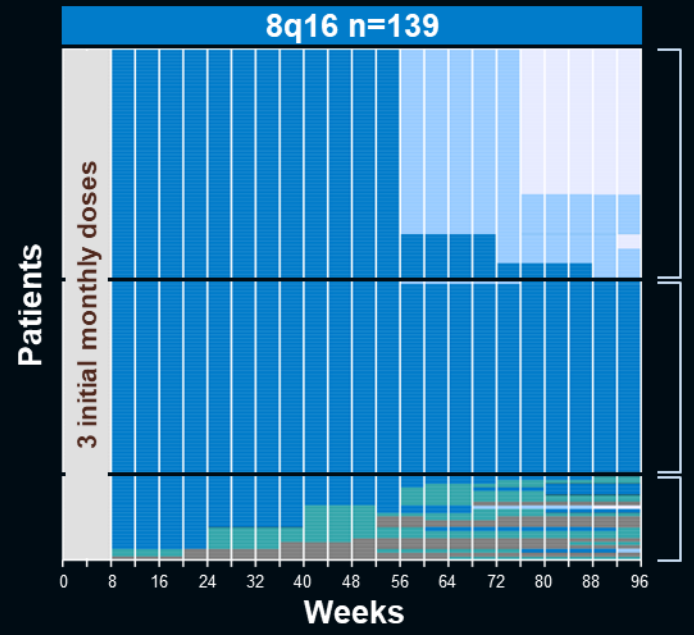
- **Criteria for interval shortening:**
  - >10-letter loss in BCVA from Week 12 due to persistent or worsening DME **AND**
  - >50-µm increase in CRT from Week 12
- Patients who met DRM criteria had dosing intervals shortened to Q8 at **Weeks 16** and **20** or by 4-week increments from **Week 24**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

Figure does not reflect all dosing options once a patient's interval is shortened or extended. Stippled boxes = initial treatment phase; X = active injection; o = sham injection.
DRM, dose regimen modification; Q8, every 8 weeks; Q24, every 24 weeks.





Definitions

Patients randomized to 8q12

Extended: Patients with dosing interval extended to Q16, Q20, or Q24 at any time and never shortened during the study

Maintained: Patients with maintained randomized dosing intervals (those extended but then shortened to Q12 or longer are included)[a]

Shortened: Patients with dosing interval shortened to Q8 at any time[b]

Patients randomized to 8q16

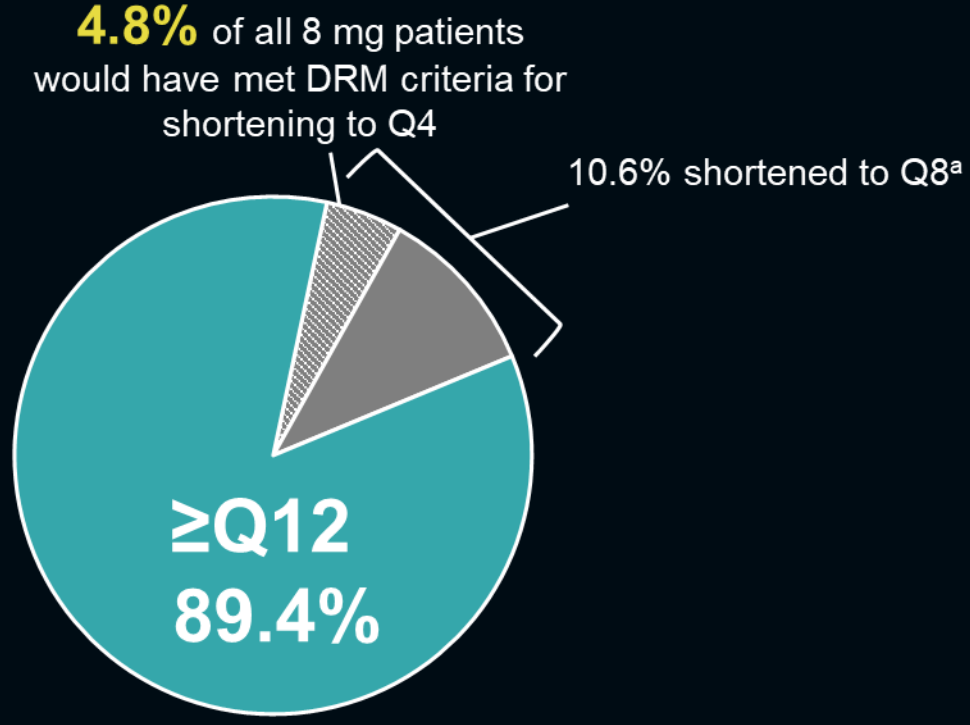
Extended: Patients with dosing interval extended to Q20 or Q24 at any time and never shortened during the study

Maintained: Patients with maintained randomized dosing intervals (those extended but then shortened to Q16 or longer are included)[a]

Shortened: Patients with dosing interval shortened to Q12 or Q8 at any time

Q12, every 12 weeks; Q16, every 16 weeks; Q20; every 20 weeks.
[a]Patients extended and then shortened back to randomized dosing interval or longer: 8q12, n=4; 8q16, n=1. [b]Patients shortened in Year 1 stayed on Q8 but could be extended in Year 2.

Exploratory Analysis of Patients Who Met DRM Criteria for Additional Theoretical Interval Shortening Through Week 96



Among patients who were shortened to Q8, 4.8% would have qualified for additional shortening to Q4

In this exploratory analysis, eyes in the all 8 mg group with dosing intervals that were shortened to Q8 through Week 96 were further evaluated to determine if the study-specified DRM criteria would have been met for further shortening to a Q4 interval. DRM criteria for interval shortening were defined as >10-letter loss in BCVA from Week 12 due to persistent or worsening DME AND >50-µm increase in CRT from Week 12.
[a]Patients whose dosing intervals were shortened based on DRM assessments at any dosing visit through Week 96. [b]Patients completing Week 96.
Q4, every 4 weeks; Q8, every 8 weeks; Q12, every 12 weeks.

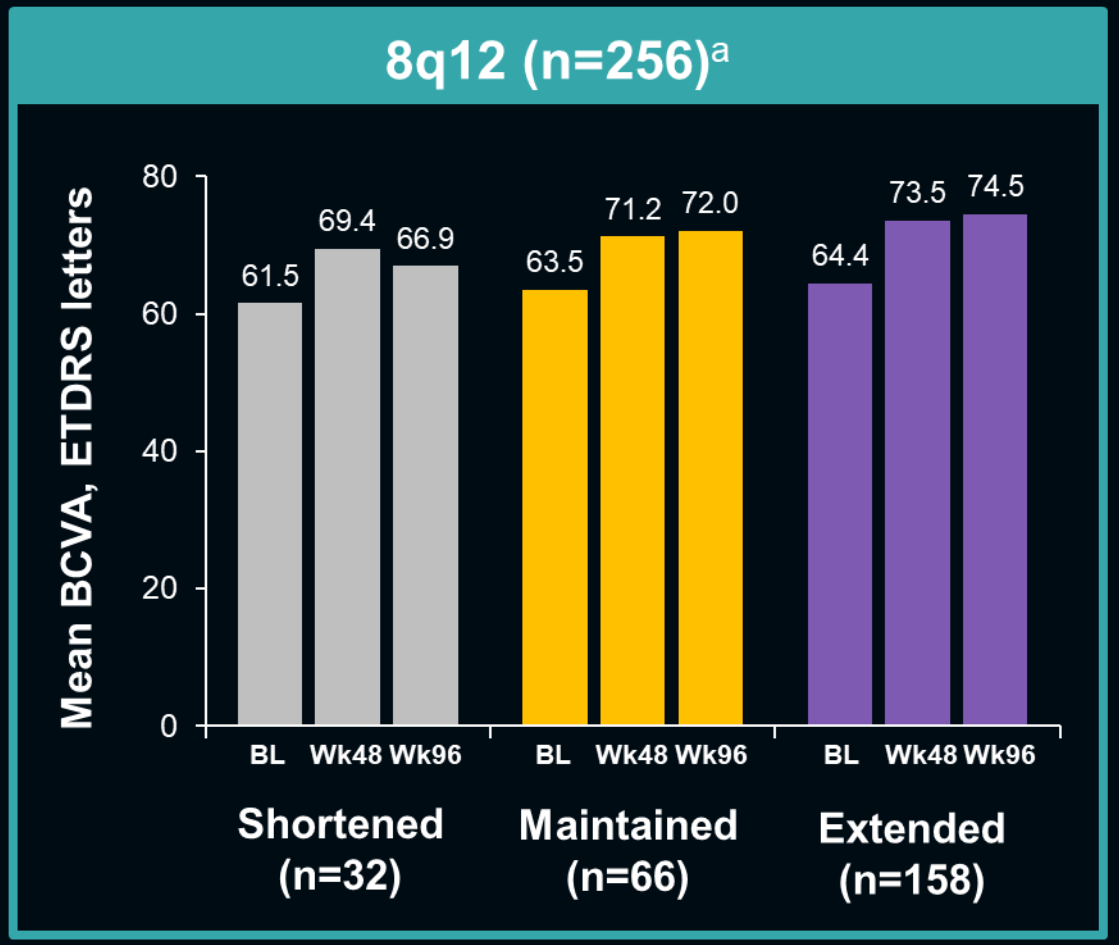
Baseline Characteristics by Dosing Interval[a]

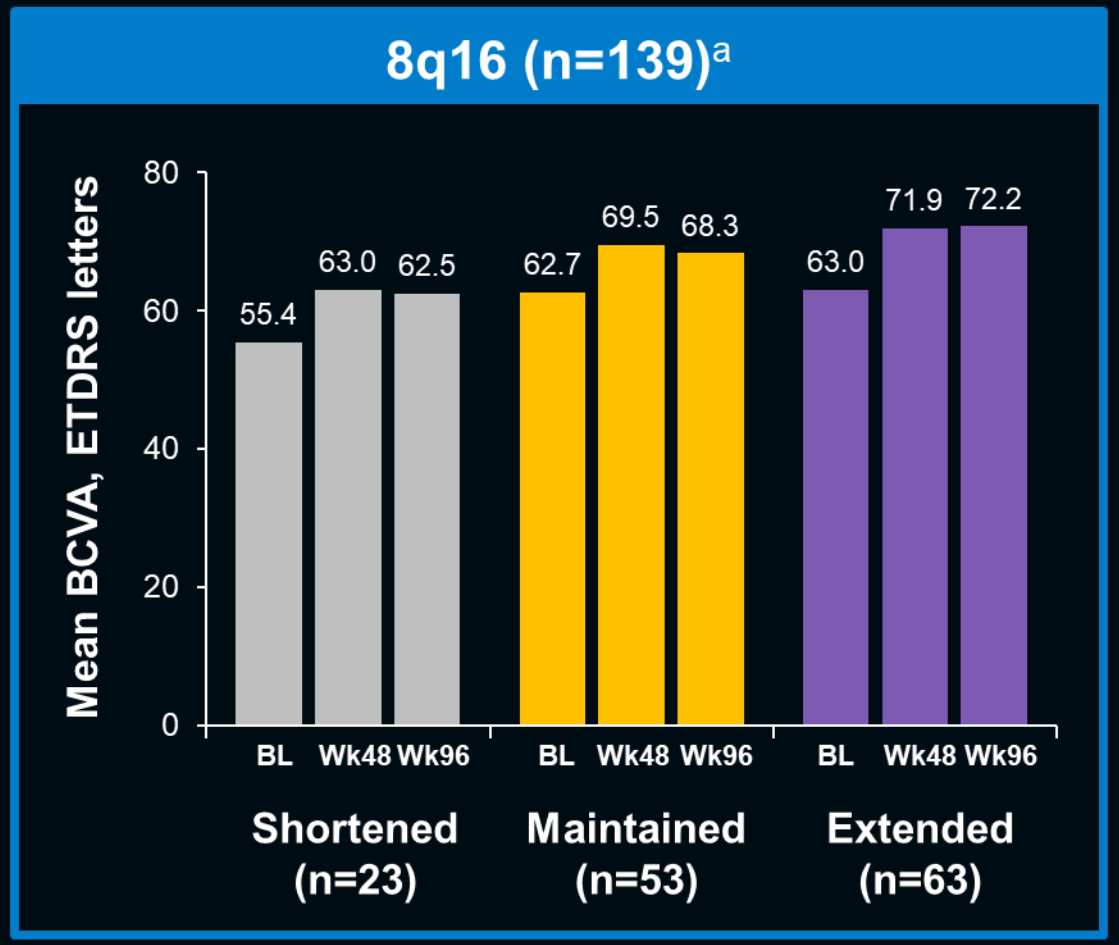
	8q12 (n=256)			8q16 (n=139)		
	Shortened (n=32)	Maintained (n=66)	Extended (n=158)	Shortened (n=23)	Maintained (n=53)	Extended (n=63)
Age, years	58.6 (13.1)	62.0 (10.7)	62.0 (11.3)	59.0 (9.2)	64.1 (8.3)	61.6 (10.0)
Male, n (%)	25 (78.1)	48 (72.7)	89 (56.3)	15 (65.2)	29 (54.7)	37 (58.7)
White, n (%)	24 (75.0)	41 (62.1)	112 (70.9)	20 (87.0)	42 (79.2)	46 (73.0)
Not Hispanic or Latino, n (%)	31 (96.9)	58 (87.9)	121 (76.6)	20 (87.0)	40 (75.5)	48 (76.2)
Type 2 diabetes, n (%)	30 (93.8)	65 (98.5)	147 (93.0)	21 (91.3)	50 (94.3)	61 (96.8)
Duration of diabetes, years	11.4 (9.1)	14.4 (9.6)	16.0 (10.3)	14.1 (10.3)	14.4 (8.5)	17.1 (12.2)
HbA1c, %	7.9 (1.5)	7.9 (1.5)	7.9 (1.5)	8.0 (1.8)	7.6 (1.4)	7.9 (1.5)
BCVA, ETDRS letters	61.5 (10.5)	63.5 (11.4)	64.4 (9.7)	55.4 (11.8)	62.7 (11.4)	63.0 (11.2)
CRT, µm	509.1 (113.6)	488.2 (131.8)	431.1 (134.2)	521.5 (141.6)	472.2 (116.0)	418.6 (100.7)
Baseline DRSS score, %						
Level 43 or better	56.3	75.8	58.9	56.5	77.4	65.1
Level 47 or worse	37.5	24.2	34.8	39.1	17.0	27.0
Ungradable	6.3	0	6.3	4.3	5.7	7.9
Prior DME treatment, n (%)	17 (53.1)	30 (45.5)	75 (47.5)	12 (52.2)	25 (47.2)	27 (42.9)

- In the aflibercept 8 mg groups, 12.5 to 16.5% of patients met DRM criteria and had their intervals shortened through Week 96

The percentage is based on the number of patients in each sub-population by treatment group as denominator. Data are mean (SD) unless otherwise indicated.
[a]Patients from the FAS who completed Week 96.
DRSS, Diabetic Retinopathy Severity Scale; FAS, full analysis set; HbA1c, hemoglobin A1c.

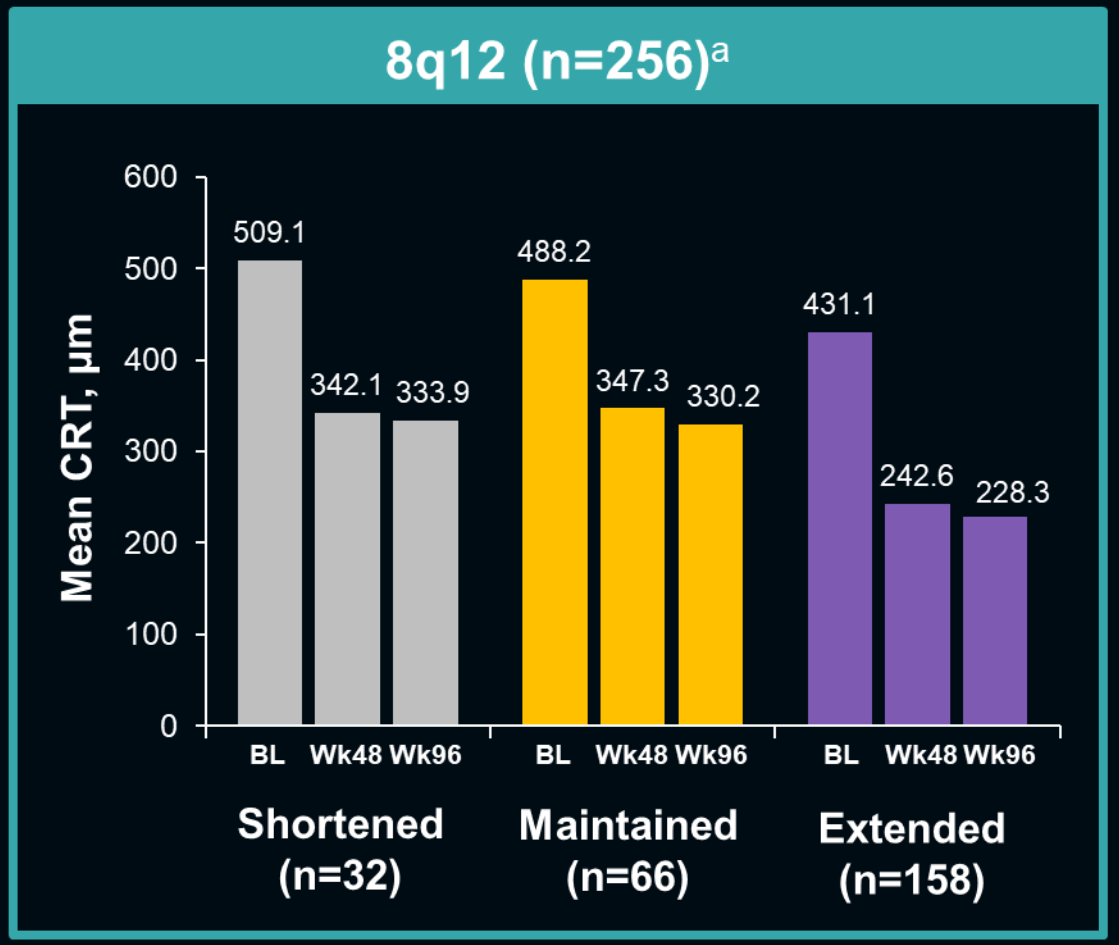
Mean BCVA at Baseline, Week 48, and Week 96 by Dosing Interval

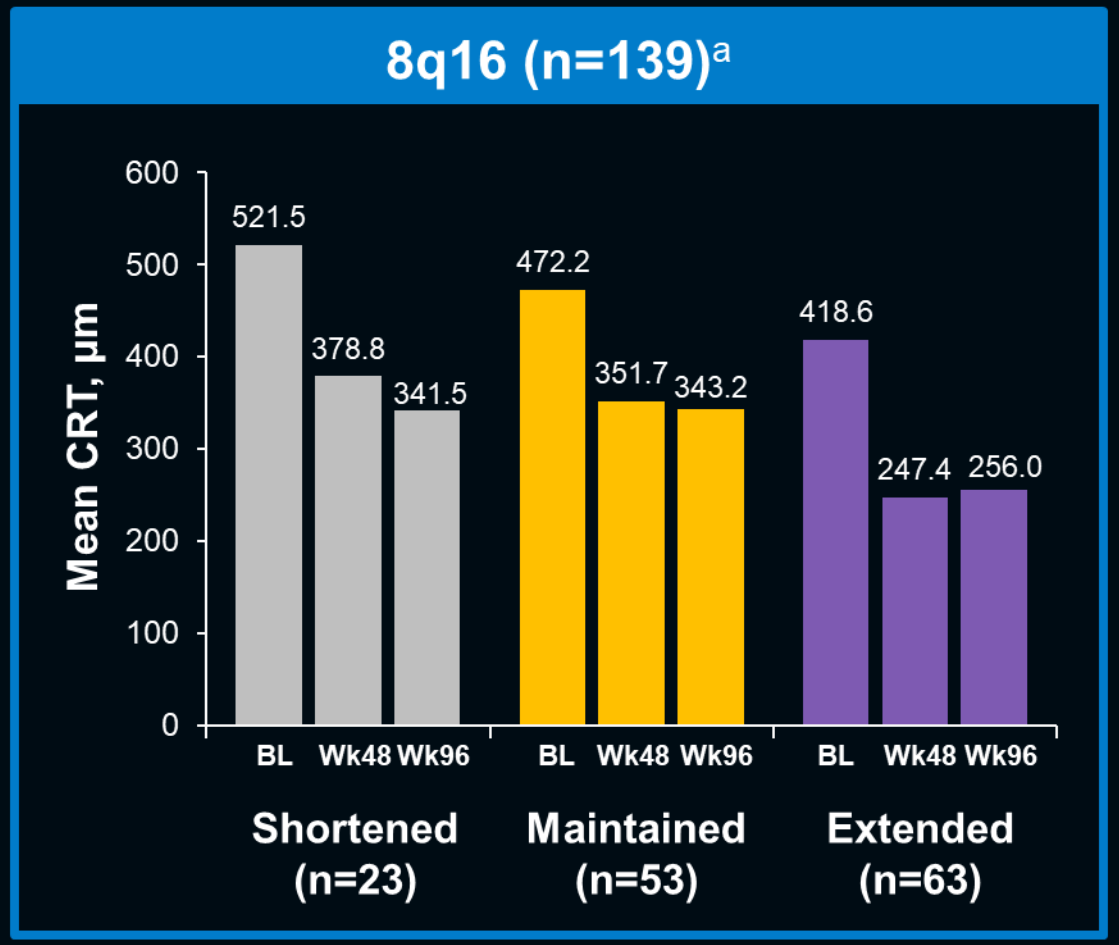




FAS, observed values (censoring data post-ICE).
[a]Patients from the FAS who completed Week 96.
BL, baseline; ICE, intercurrent event; Wk, Week.

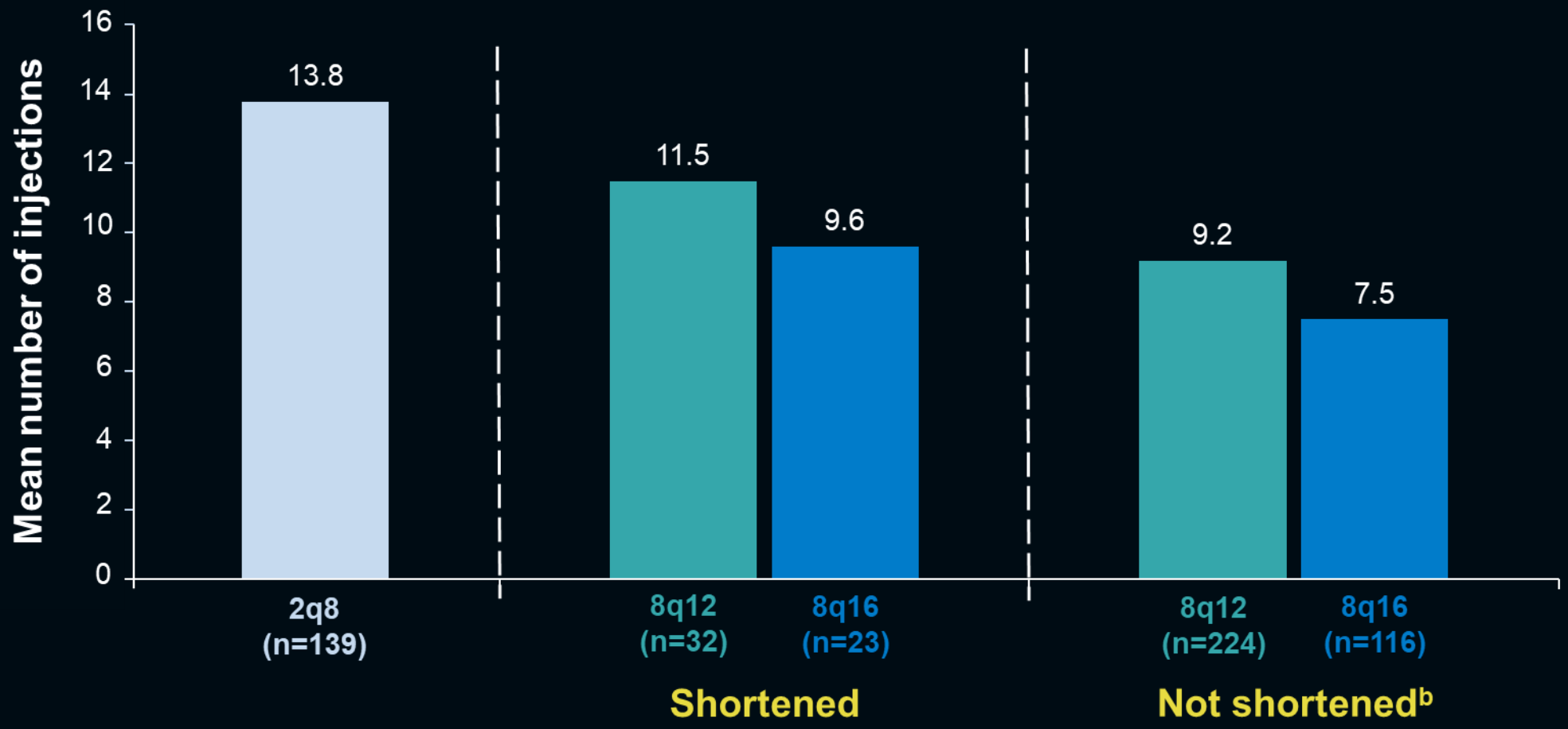
Mean CRT at Baseline, Week 48, and Week 96 by Dosing Interval





FAS, observed values (censoring data post-ICE).
[a]Patients from the FAS who completed Week 96.

Treatment Exposure Through Week 96 by Dosing Subcohort[a]



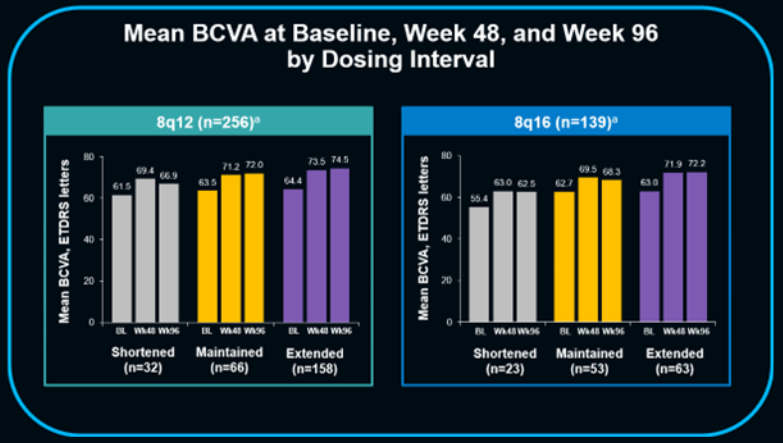
[a]Patients from the FAS who completed Week 96. [b]Maintained and Extended combined.

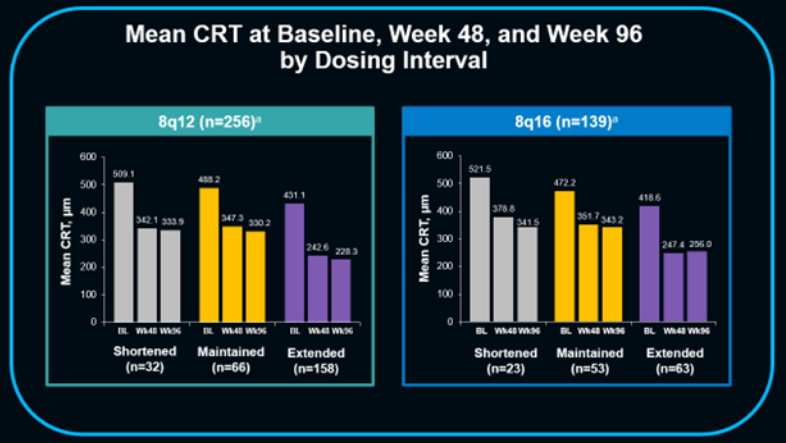
Treatment-Emergent Adverse Events Through Week 96[a]

	Shortened			Not Shortened[b]			
	8q12 (n=32)	8q16 (n=23)	All 8 mg (n=55)	2q8 (n=139)	8q12 (n=224)	8q16 (n=116)	All 8 mg (n=340)
Intraocular pressure increased, n	3	0	3	6	4	2	6
Intraocular inflammation, n	1	0	1	2	2	1	3
Anterior chamber cell	1	0	1	1	0	0	0
Iridocyclitis	0	0	0	1	0	1	1
Uveitis	0	0	0	1	1	0	1
Vitreal cells	0	0	0	0	1	0	1
APTC event, n	3	2	5	7	8	4	12

[a]Patients from the SAF who completed Week 96. [b]Maintained and Extended combined.
APTC, Anti-Platelet Trialists' Collaboration.

Conclusions





- Dosing intervals were shortened to every 8 weeks for at least 1 interval in ≤16.5% of patients receiving aflibercept 8 mg through Week 96
- Patients treated with aflibercept 8 mg with shortened, maintained, or extended dosing intervals had meaningful BCVA gains and CRT improvements at Week 96 with a comparable safety profile to 2q8