Baseline Characteristics and Outcomes of Patients Treated with Aflibercept 8 mg at Shortened, Maintained, or Extended Dosing Intervals Through 96 Weeks in PHOTON

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PHOTON Study Design

Treatment-naive and previously treated patients with center-involved DME[a]

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

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

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

	Year 1													Year 2										
	Day 1	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 28	Wk 32	Wk 36	Wk 40	Wk 44	Wk 48	Wk 52	Wk 56	Wk 60	Wk 64	Wk 68	Wk 72	Wk 76	Wk 80	Wk 84	Wk 88	Wk 92	Wk 96
2q8	X	X	X	X	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	–
8q12	X	X	X	o	o[a]	X[a]	o	o	X[a]	o	o	X[a]	o	o	X[a,b]	o	o	X[a,b]	o	o	X[a,b]	o	o	X[a,b]	–
8q16	X	X	X	o	o[a]	o[a]	X[a]	o	o	o	X[a]	o	o	o	X[a,b]	o	o	o	X[a, b]	o	o	o	X[a,b]	o	–

Primary endpoint at Week 48
Mean change in BCVA (non-inferiority)

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

[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

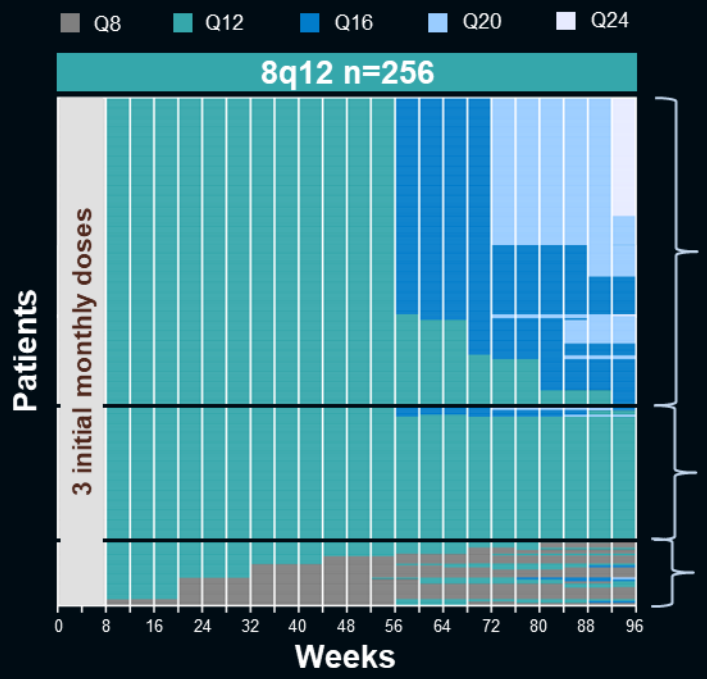
[b]DRM: Interval Extension During Year 2

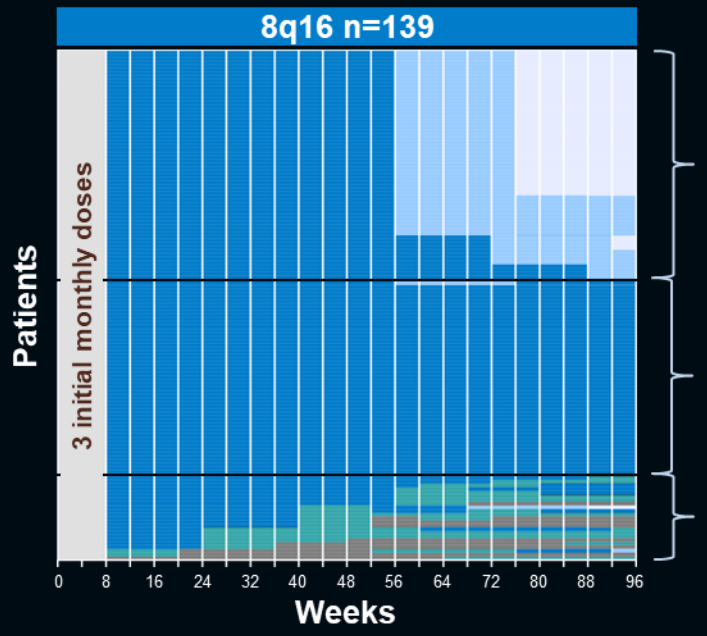
- **Criteria for interval extension:**
  - <5-letter loss in BCVA from Week 12 **AND**
  - CRT <300 µm (or <320 µm on Spectralis)
- Patients who met DRM criteria beginning at **Week 52** had dosing intervals extended by 4-week increments
  - The maximum assigned interval was Q24

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.
2q8, 2 mg every 8 weeks; 8q12, 8 mg every 12 weeks; 8q16, 8 mg every 16 weeks; BCVA, best-corrected visual acuity; CRT, central retinal thickness; DME, diabetic macular edema; DRM, dose regimen modification; Q8, every 8 weeks; Q24, every 24 weeks; Wk, week.

Objective

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





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 dosing interval maintained (including those extended then shortened back to no less than Q12[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 dosing interval maintained (including those extended then shortened back to no less than Q16[a])

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

[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.
Q12, every 12 weeks; Q16, every 16 weeks; Q20; every 20 weeks.

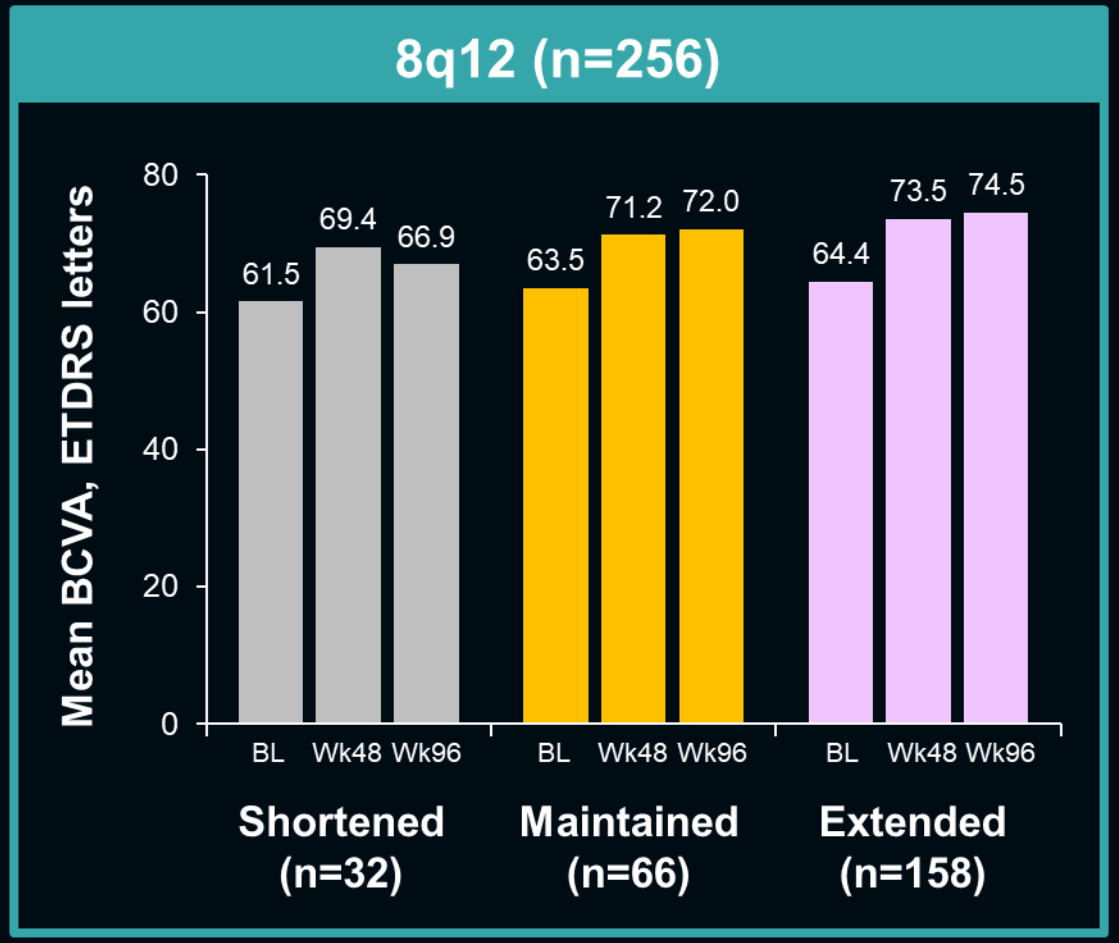
Baseline Characteristics by Dosing Interval[a]

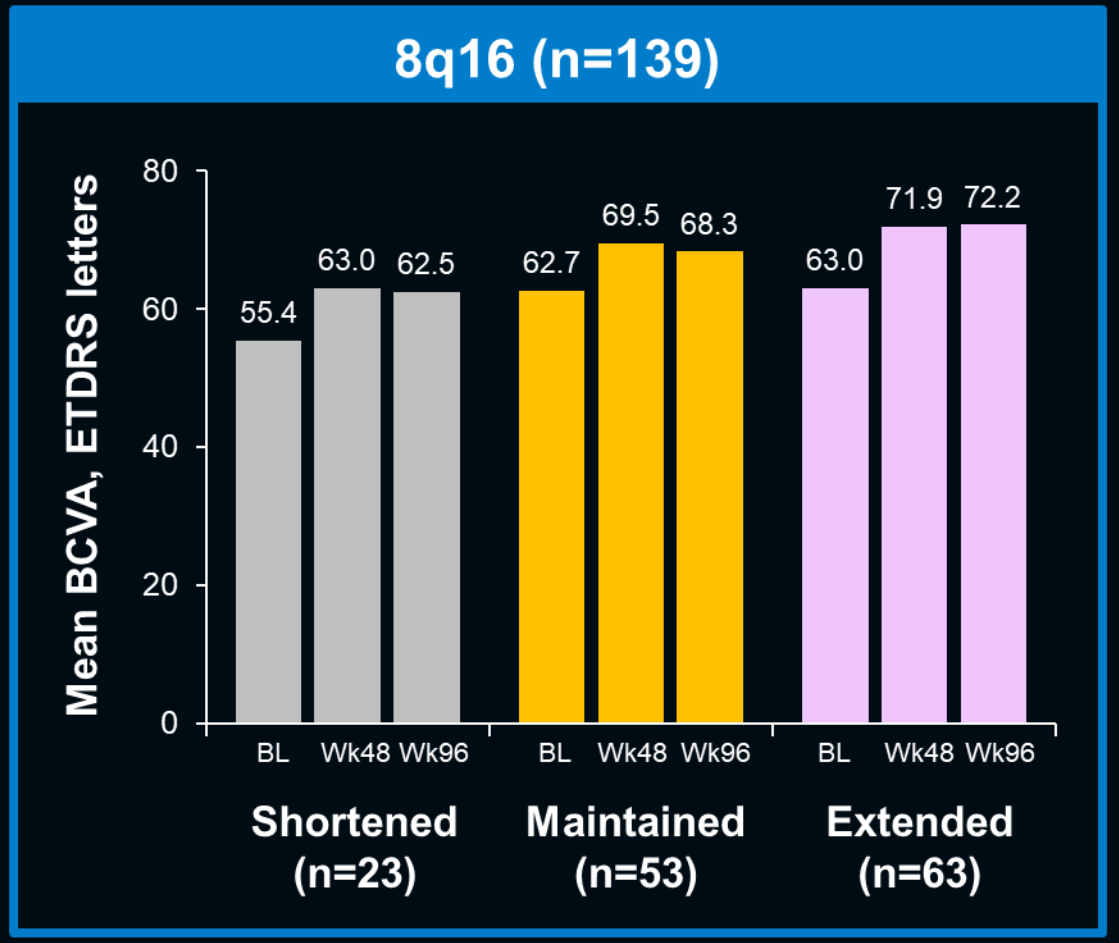
	8q12 (n=256)			8q16 (n=139)		
	Shortened (n=32)	Maintained (n=66)	Extended (n=158)	Shortened (n=23)	Maintained (n=53)	Extended (n=63)
Age, years	58.6 (13.1)	62.0 (10.7)	62.0 (11.3)	59.0 (9.2)	64.1 (8.3)	61.6 (10.0)
Male, n (%)	25 (78.1)	48 (72.7)	89 (56.3)	15 (65.2)	29 (54.7)	37 (58.7)
White, n (%)	24 (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, 13% to 17% of patients met DRM criteria and had their intervals shortened through Week 96

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

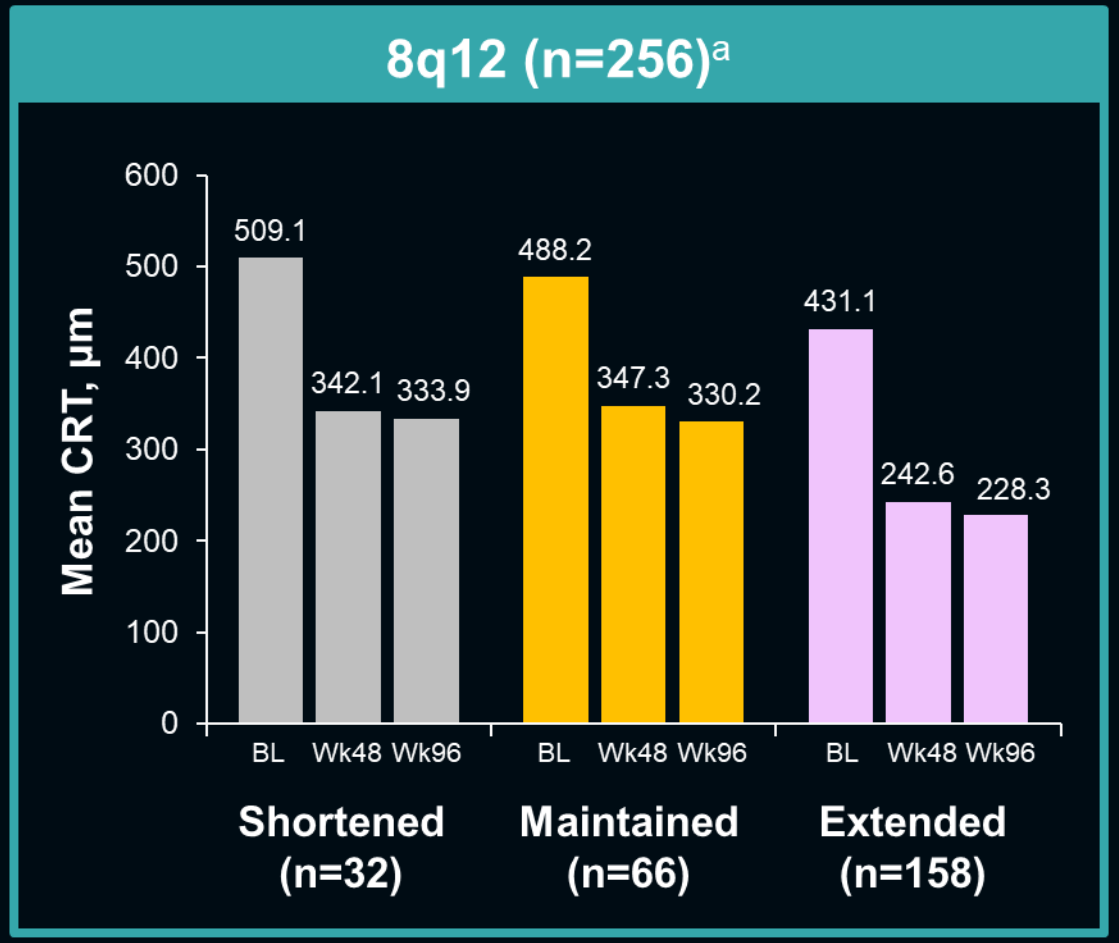
Mean BCVA at Baseline, Week 48, and Week 96 by Dosing Interval

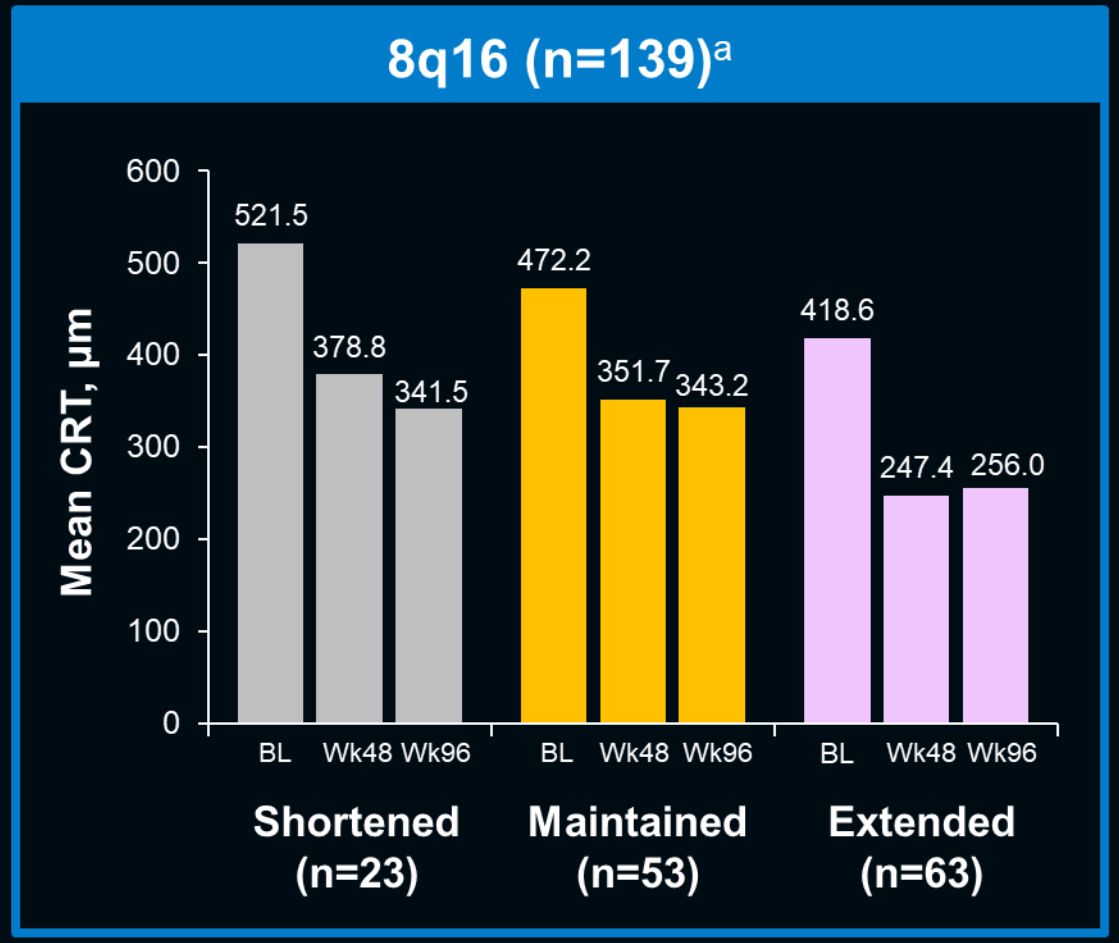




FAS, patients who completed Week 96 visit.
BL, baseline.

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

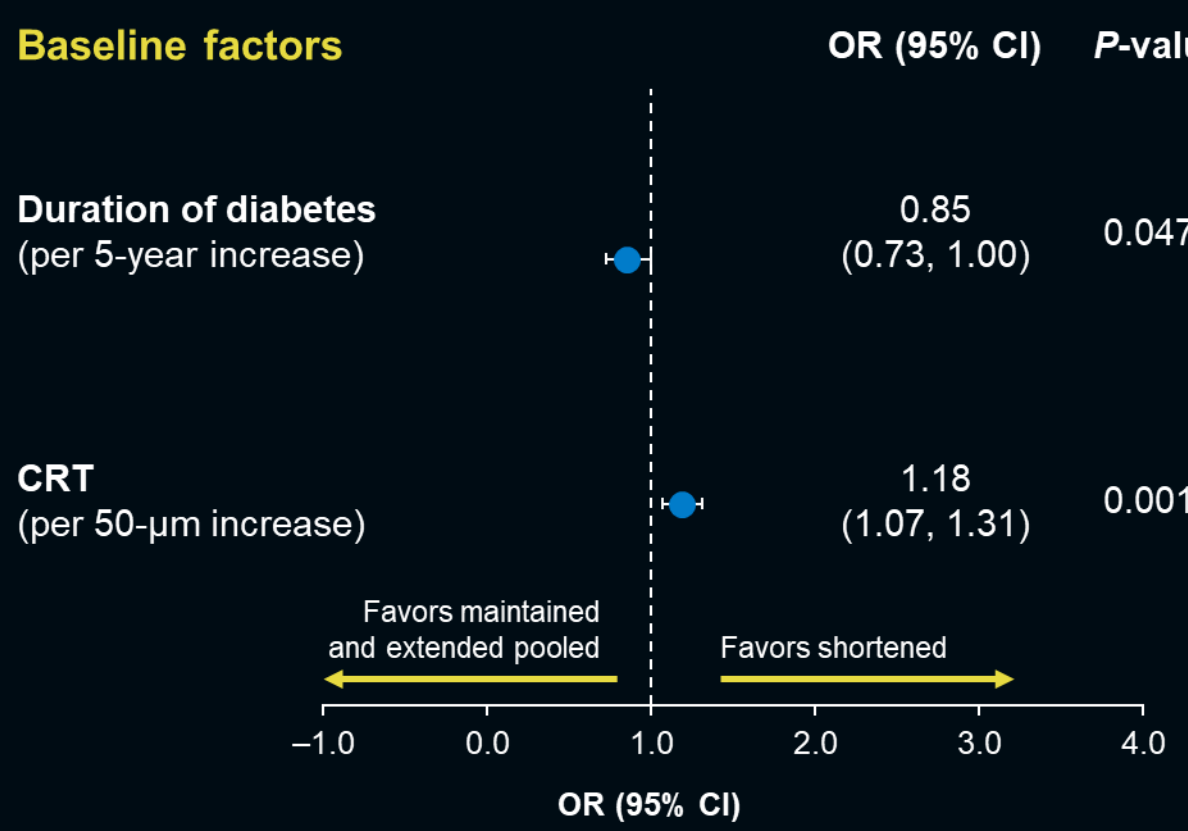




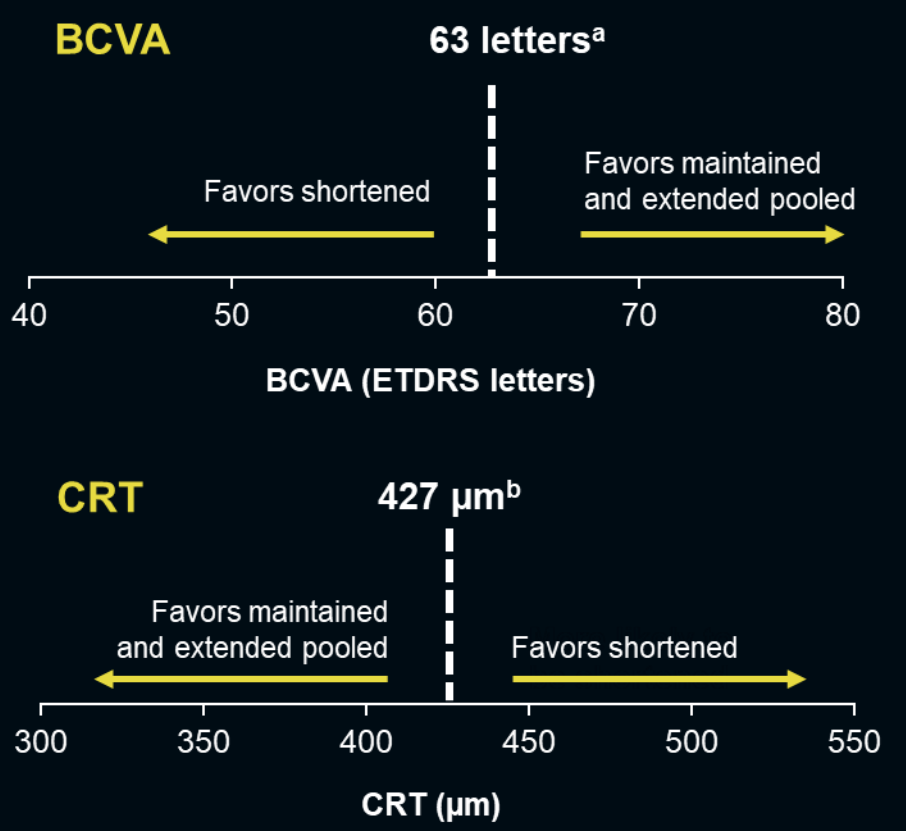
FAS, observed values (censoring data post–intercurrent event).
[a]Patients from the FAS who completed Week 96.

Baseline Factors Associated With Interval Shortening (vs Maintenance/Extension) Through Week 96

Multivariate analysis



ROC analysis



Patients maintained or extended through Week 96 were used as the reference. Inferential statistics were calculated from a logistic regression model. Age (per 10-year increase), duration of diabetes (per 5-year increase),
BCVA (per 5-letter decrease) and CRT (per 50-µm increase) were included in the stepwise logistic regression process.
[a]Area under the curve = 0.6301. [b]Area under the curve = 0.6703.
OR, odds ratio; ROC, receiver operating characteristic.

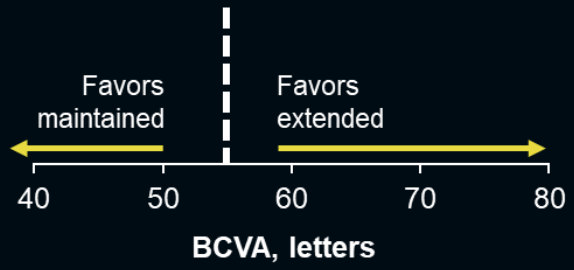
Baseline Factors Predicting Interval Extension (vs Maintenance) Through Week 96

Univariate analysis

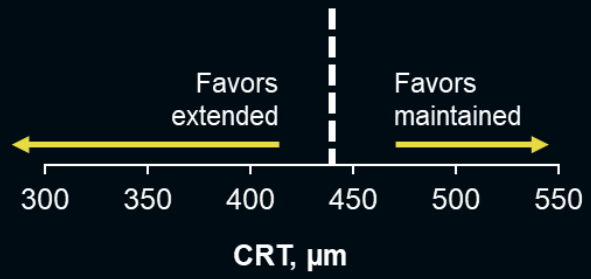
Baseline factors	N	n	OR (95% CI)	*P*-value
Age (per 10-year increase)	340	–	0.91 (0.73, 1.12)	0.3747
Sex (male vs female)	340	–	0.72 (0.46, 1.15)	0.1685
Race (White vs non-White)	340	–	1.09 (0.67, 1.77)	0.7355
Diabetes type (type 2 vs type 1)	340	–	0.56 (0.18, 1.75)	0.3157
HbA1c (per 1% increase)	337	–	1.06 (0.91, 1.23)	0.4664
Duration of diabetes (per 5-year increase)	339	–	1.10 (0.98, 1.23)	0.0972
BMI (per 5-kg/m^2 increase)	340	–	0.87 (0.73, 1.04)	0.1297
BCVA (per 5-letter decrease)	340	–	0.96 (0.87, 1.07)	0.4612
CRT (per 50-µm increase)	**340**	**–**	**0.85 (0.77, 0.93)**	**0.0004**
Prior DME treatment (yes vs no)	340	157	1.00 (0.64, 1.56)	0.9909
History of hypertension (yes vs no)	340	262	0.78 (0.45, 1.34)	0.3728

ROC analysis

BCVA 55 letters[a]



CRT 440 µm[b]



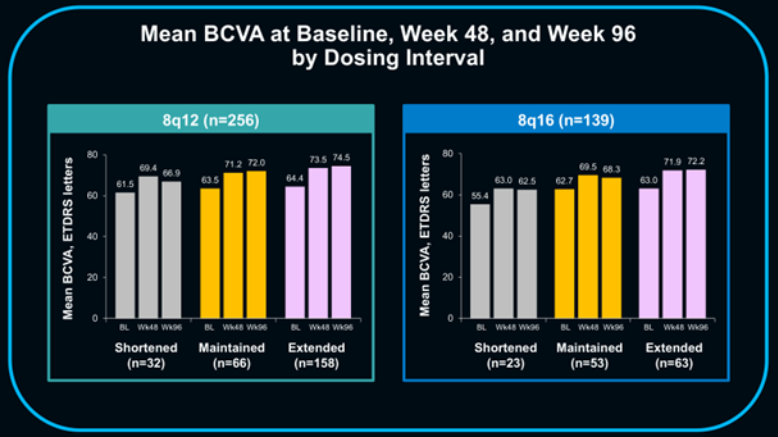
Patients maintained through Week 96 were used as the reference. Inferential statistics were calculated from a logistic regression model.
[a]Area under the curve = 0.5106. [b]Area under the curve = 0.6394.
BMI, body mass index.

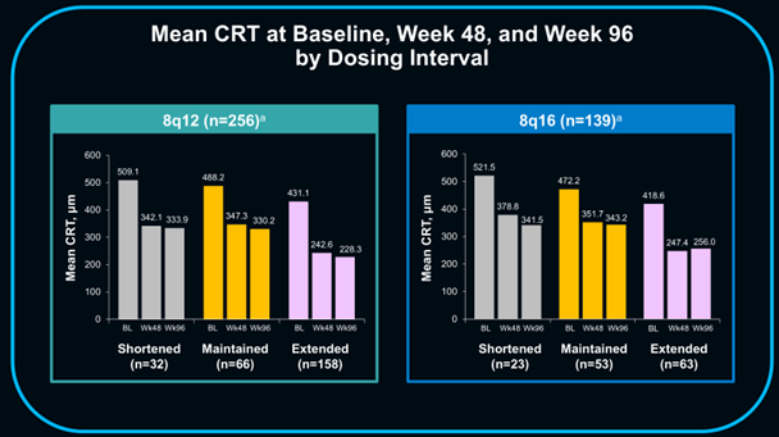
Treatment-Emergent Adverse Events Through Week 96

	Shortened			Not shortened[a]			
	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

Safety analysis set completing Week 96 visit.
[a]Patients in the maintained and extended groups were combined.
APTC, Anti-Platelet Trialists' Collaboration.

Conclusions





- Dosing intervals were shortened at any time in ≤17% of patients receiving aflibercept 8 mg through Week 96
- Shorter duration of diabetes and higher CRT at baseline were predictors of dosing interval shortening whereas lower CRT at baseline was predictive of interval extension
- Patients treated with aflibercept 8 mg achieved meaningful improvements in BCVA and CRT at Week 96 with a comparable safety profile to 2q8, regardless of dosing interval status