Baseline Characteristics of Patients Who Did or Did Not Maintain 12- & 16-Week Aflibercept 8 mg Dosing Intervals in the Phase 2/3 PHOTON Trial

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PHOTON: Study Design and Dosing Schedule

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DME

Multicenter, randomized, double-masked study in patients with DME*
Randomized 1 (2q8) : 2 (8q12) : 1 (8q16)
Primary endpoint at Week 48: Mean change in BCVA (non-inferiority)

Key secondary endpoint: Proportion of patients with ≥2-step improvement in DRSS at Week 48

	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
2q8 (n=167)	X	X	X	X	X	o	X	o	X	o	X	o	X
8q12 (n=328)	X	X	X	o	o	X	o	o	X	o	o	X	o
8q16 (n=163)	X	X	X	o	o	o	X	o	o	o	X	o	o

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

DRM Criteria for Shortening Dosing Interval[a]

- >10-letter loss in BCVA due to persistent or worsening DME

AND

- >50-micron increase in CST

DRM in Year 1

- Intervals can only be shortened
- Multiple opportunities to shorten interval
- Minimum interval for all patients was Q8

Week 16 and 20: Patients on 8q12 and 8q16 meeting DRM criteria shortened to Q8

Week 24: Patients on 8q16 meeting DRM criteria shortened to Q12

Week 32 and 44 for 8q12 and Week 40 for 8q16: Treatment interval shortened by 4 weeks for patients meeting DRM criteria

Stippled boxes = initial treatment phase; X = active injection; o = sham injection. Note: Figure does not reflect all dosing options once a patient is shortened.
[a]All assessments compared to Week 12.
2q8, aflibercept 2 mg every 8 weeks; 8q12, aflibercept 8 mg every 12 weeks; 8q16, aflibercept 8 mg every 16 weeks; BCVA, best-corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; DRM, dose regimen modification; DRSS, Diabetic Retinopathy Severity Scale; Q8, every 8 weeks; Q12, every 12 weeks; Wk, week.

PHOTON: 48-Week BCVA
Primary Endpoint Met in Both 8 mg Groups

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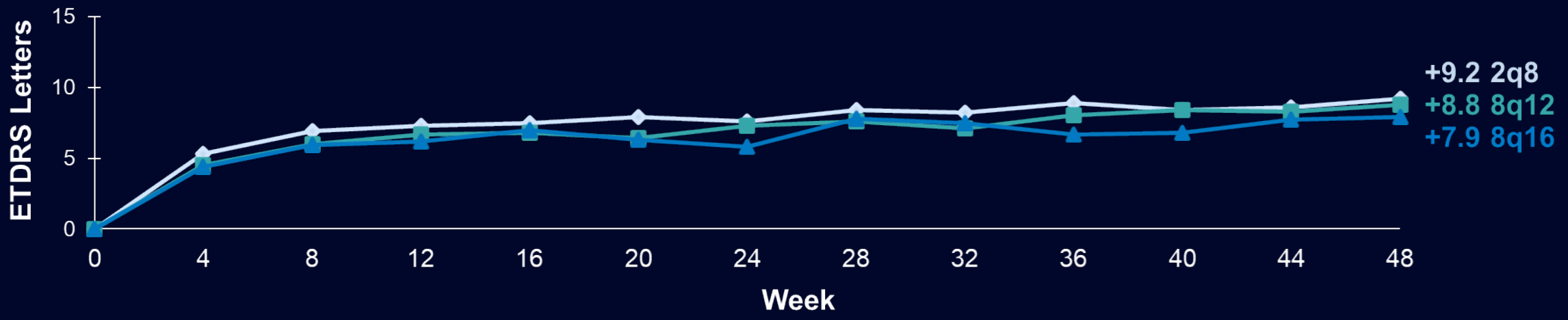
DME

BCVA Change from Baseline[a]



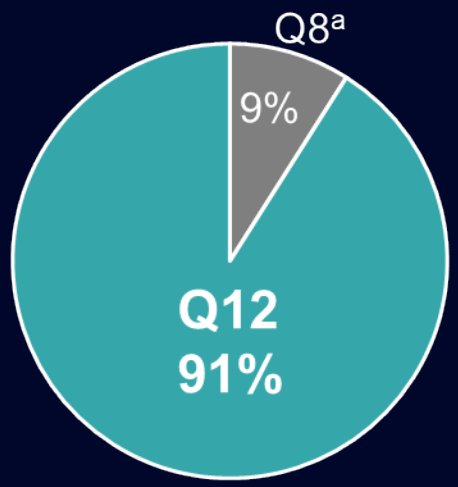
	LS mean change from BL at Week 48 (MMRM)	Diff. in LS means vs. 2q8	2-sided 95% CI	1-sided test for non-inferiority at 4-letter margin
2q8	8.7			
8q12	8.1	-0.57	-2.26, 1.13	p < 0.0001
8q16	7.2	-1.44	-3.27, 0.39	p = 0.0031

[a]Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at baseline).
BL, baseline; CI, confidence intervals; Diff, difference; ETDRS, Early Treatment Diabetic Retinopathy Study; FAS, full analysis set; ICE, intercurrent event; LS, least squares; MMRM, mixed model for repeated measures.

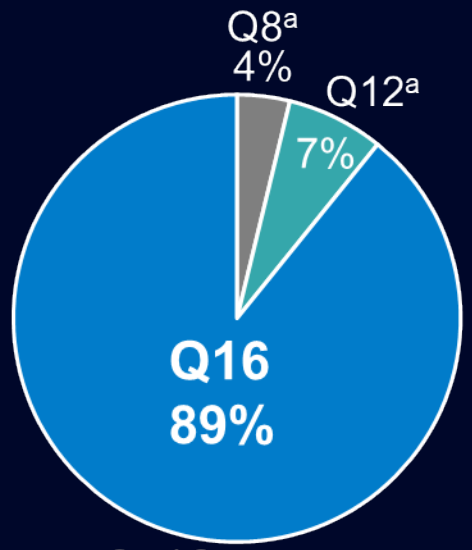
Proportion of 8 mg Patients Maintaining Q12- and Q16-Week Intervals Through Week 48

DME

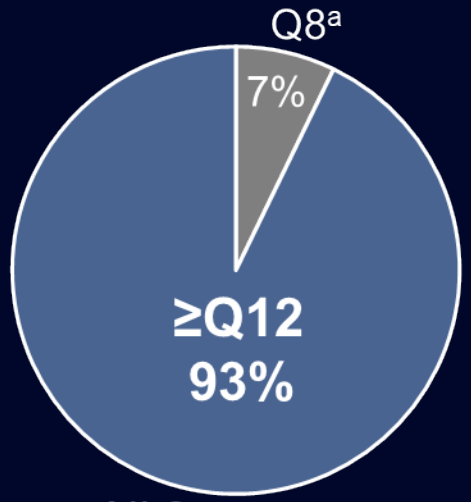
93% of 8 mg patients maintained dosing intervals ≥12 weeks



8q12 (n=300)[b]



8q16 (n=156)[b]



All 8 mg (n=456)[b]

Objectives of this analysis:

- To describe baseline characteristics of patients with maintained vs. shortened dosing intervals
- To identify baseline characteristics associated with shortened dosing intervals
- To evaluate visual and anatomic outcomes at Week 48 in patients with maintained vs. shortened dosing intervals

[a]Patients shortened based on DRM assessments at some point through Week 48.
[b]Patients completing Week 48.

Baseline Demographics by Dosing Interval

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DME

	8q12 (n=300)[a]		8q16 (n=156)[a]	
	Maintained	Shortened	Maintained	Shortened
n	273; 91.0%	27; 9.0%	139; 89.1%	17; 10.9%
Age (years)	62.2 (10.9)	59.1 (13.9)	62.0 (9.6)	60.1 (9.9)
Sex (%)				
Female	36.3	25.9	41.0	29.4
Male	63.7	74.1	59.0	70.6
Race (%)[b]				
White	69.6	70.4	77.0	88.2
Black or African American	10.3	14.8	6.5	0
Asian	15.8	14.8	14.4	11.8
Other[c]	2.9	0	0.7	0
Not reported	1.5	0	1.4	0

Data are mean (SD) unless otherwise indicated.
[a]Patients from the FAS who completed Week 48.
[b]The sum of proportions may not equal 100% due to rounding.
[c]Other includes American Indian or Alaskan Native, Native Hawaiian or other Pacific Islander, and Multiple.

Baseline Demographics by Dosing Interval

	8q12 (n=300)[a]		8q16 (n=156)[a]	
	Maintained	Shortened	Maintained	Shortened
n	273; 91.0%	27; 9.0%	139; 89.1%	17; 10.9%
Ethnicity (%)[b]				
Hispanic or Latino	16.1	3.7	23.0	5.9
Not Hispanic or Latino	81.3	96.3	75.5	88.2
Not reported	2.6	0	1.4	5.9
Type 2 diabetes (%)	94.5	92.6	95.0	94.1
Duration of diabetes (years)	15.5 (10.1)	11.1 (9.7)	15.6 (10.5)	15.8 (11.0)
NEI VFQ-25 total score	77.1 (17.3)	76.1 (16.4)	78.7 (15.5)	72.4 (16.8)
BMI (kg/m^2)	30.3 (6.1)	29.3 (6.6)	31.1 (6.3)	30.5 (4.8)
Hemoglobin A1c (%)	8.0 (1.5)	7.8 (1.4)	7.9 (1.5)	7.8 (1.9)
Hemoglobin A1c category (%)[b]				
≤8%	57.5	70.4	63.3	70.6
>8%	41.8	29.6	35.3	29.4

Data are mean (SD) unless otherwise indicated.
[a]Patients from the FAS who completed Week 48.
[b]The sum of proportions may not equal 100% due to rounding or missing values.
BMI, body mass index; NEI VFQ-25, National Eye Institute Visual Functioning Questionnaire-25.

Baseline Ocular Characteristics by Dosing Interval

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DME

	8q12 (n=300)[a]		8q16 (n=156)[a]	
	Maintained	Shortened	Maintained	Shortened
n	273; 91.0%	27; 9.0%	139; 89.1%	17; 10.9%
BCVA (ETDRS letters)	63.9 (10.1)	59.4 (10.0)	62.7 (11.2)	53.7 (12.8)
CST (μm)	444.9 (129.8)	511.4 (117.5)	447.1 (112.5)	534.8 (134.3)
Baseline DRSS score (%)				
Level 43 or better	61.2	51.9	66.9	58.8
Level 47 or worse	33.7	40.7	26.6	41.2
Ungradable	5.1	7.4	6.5	0
Prior DME treatment, n (%)	42.5	55.6	44.6	47.1

Compared with patients who maintained their randomized dosing intervals, those whose dosing intervals were shortened had on average **lower** BCVA and **greater** CST at baseline

Data are mean (SD) unless otherwise indicated.
[a]Patients from the FAS who completed Week 48.

Univariable Analysis: Baseline Characteristics Associated with the Incidence of Dosing Interval Shortening

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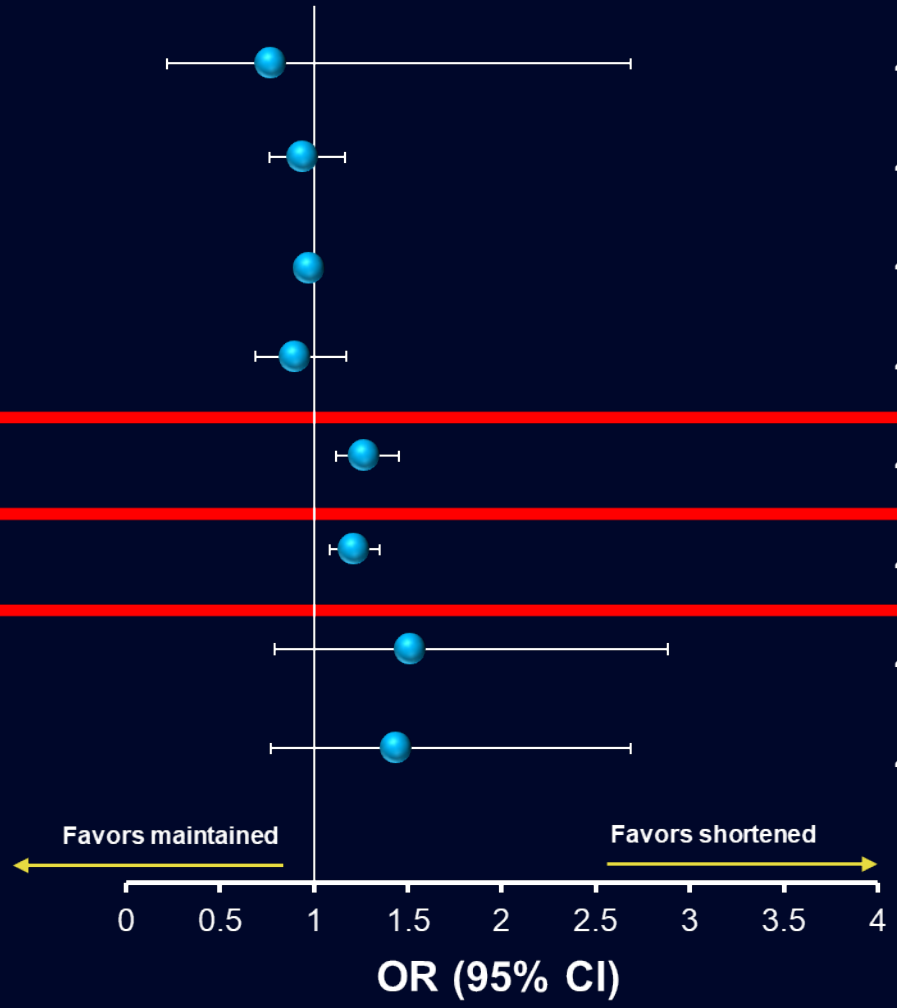
DME



	N	n	OR (95% CI)	*P*-value
Diabetes type (Type 2 vs. Type 1)	456	431	0.77 (0.22, 2.69)	0.6827
Hemoglobin A1c (per 1% increase)	452	–	0.94 (0.76, 1.17)	0.5871
Duration of diabetes (per 1-year increase)	454	–	0.97 (0.94, 1.01)	0.1048
BMI (per 5 kg/m^2 increase)	455	–	0.90 (0.69, 1.17)	0.4273
BCVA (per 5-letter decrease)	456	–	1.27 (1.12, 1.45)	0.0003
CST (per 50 µm increase)	455	–	1.21 (1.09, 1.35)	0.0005
DRSS (≥47-<90 vs ≤43)	431	147	1.51 (0.79, 2.89)	0.2101
Prior DME treatment (Yes vs No)	456	201	1.44 (0.77, 2.68)	0.2513

OR, odds ratio.
N, number of patients evaluated for the specified baseline characteristic; n, number of patients in the first specified category.

Multivariable Analysis: Baseline Characteristics Associated with the Incidence of Dosing Interval Shortening

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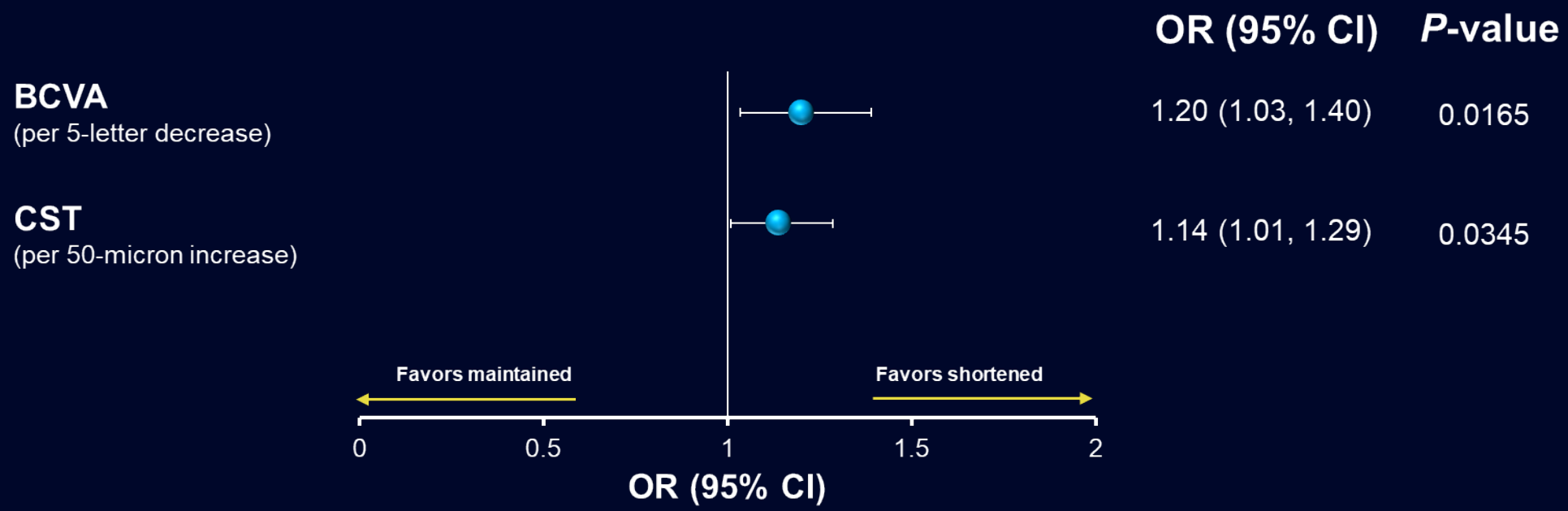
DME

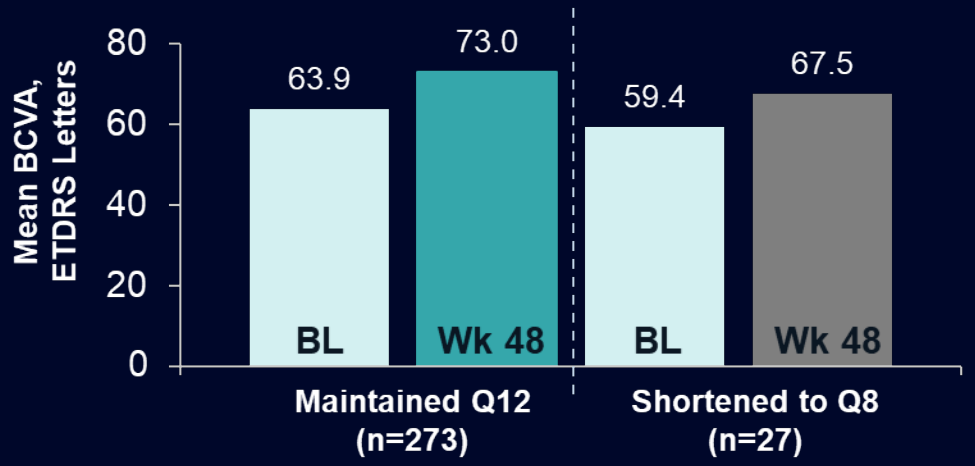


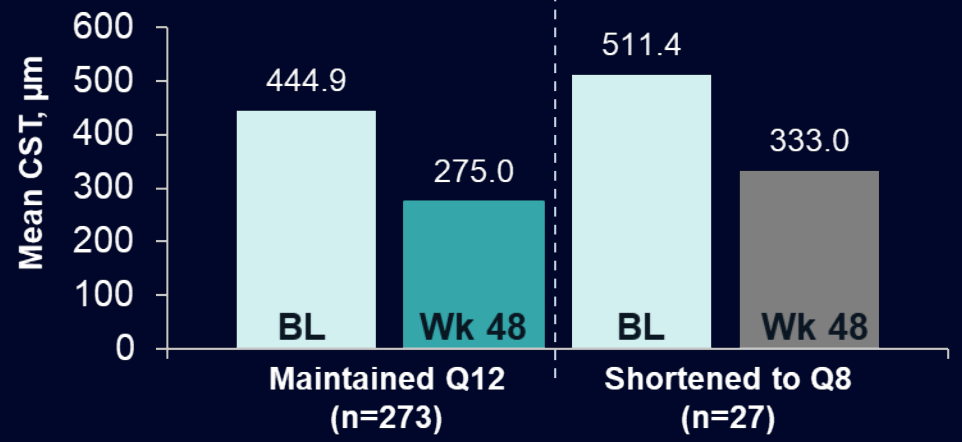
A subsequent ROC analysis of pooled data for aflibercept 8 mg demonstrated that patients with BCVA ≤58 letters or CST ≥474 µm at baseline were more likely to have shortened dosing intervals in this trial

Absolute BCVA and CST at Baseline and Week 48 by Dosing Interval

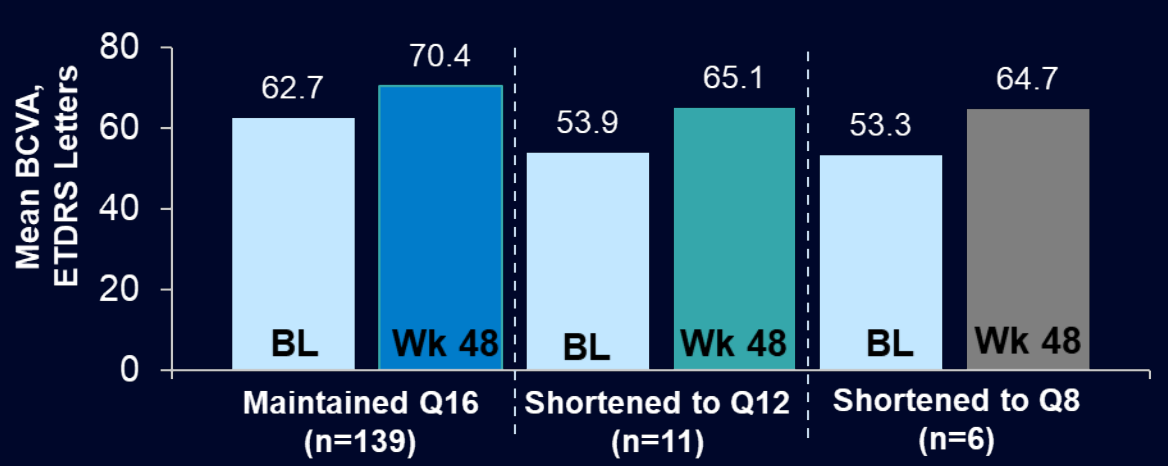
DME

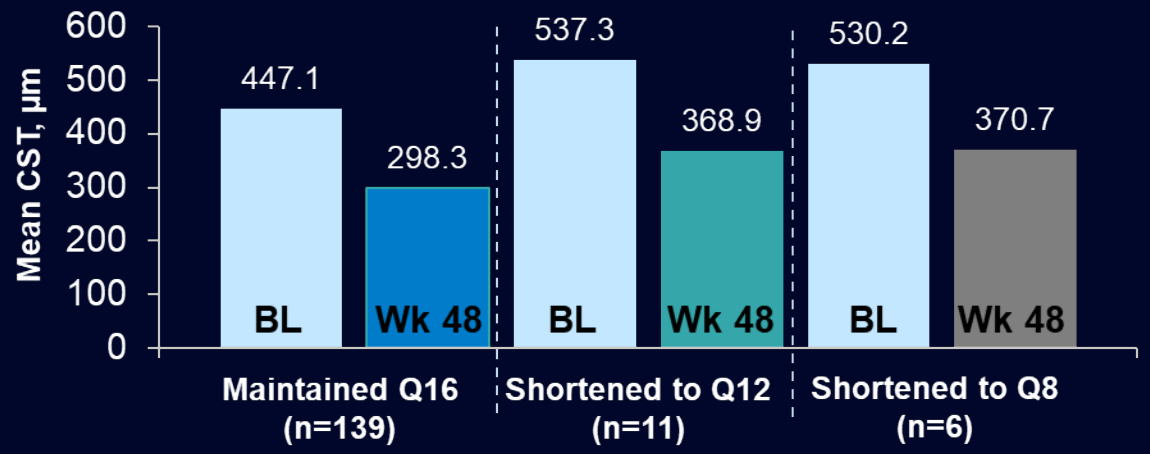
8q12 (n=300)[a]





8q16 (n=156)[a]





[a]Patients from the FAS who completed Week 48.
FAS, observed values (censoring data post-ICE).

Conclusions

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DME

- Aflibercept 8q12 and 8q16 demonstrated non-inferior BCVA gains compared to aflibercept 2q8 at Week 48, with a large majority of patients maintaining their randomized 12- or 16-week dosing intervals
  - Dosing intervals were shortened in approximately 10% of patients
- Lower BCVA and greater CST at baseline were associated with shortened dosing intervals in patients receiving aflibercept 8 mg in this trial
- Patients treated with aflibercept 8 mg with shortened dosing intervals had meaningful BCVA gains and CST improvements at Week 48, although absolute BCVA and CST values at Week 48 were not equivalent to those of patients with maintained dosing intervals