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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Disclosures

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DME

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PHOTON: Study Design and Dosing Schedule

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Multi-center, randomized, double-masked study in patients with DME[a]
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: Aflibercept 2 mg arm received 5 initial monthly injections versus aflibercept 8 mg arms, which received only 3 initial monthly injections

DRM Criteria for Shortening Dosing Interval

- **>10-letter loss in BCVA compared with Week 12, due to persistent or worsening DME**

AND

- **>50 µm increase in CST compared with Week 12**

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's dosing interval is shortened.
[a]Treatment naïve and pre-treated.
CST, central subfield thickness; DRM, dose regimen modification; DME, diabetic macular edema.

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

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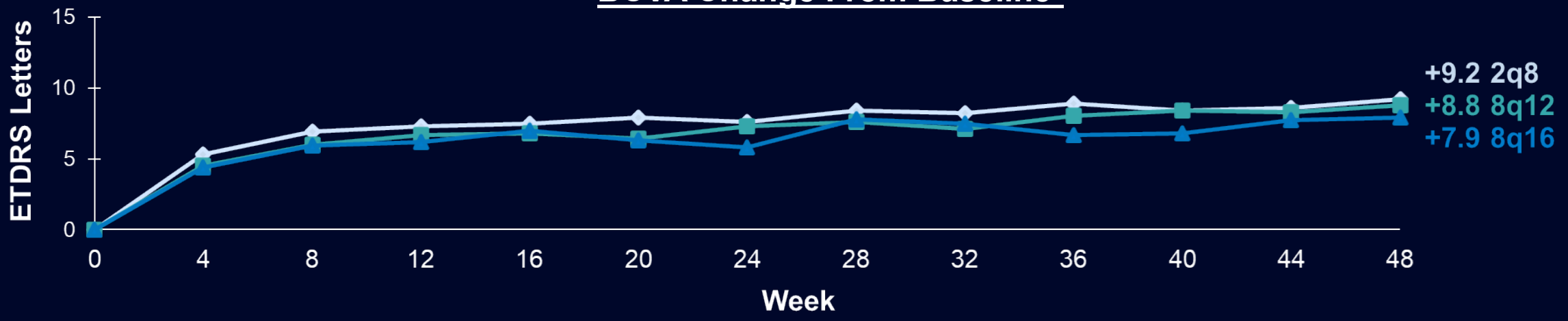
DME

BCVA Change From Baseline[a]



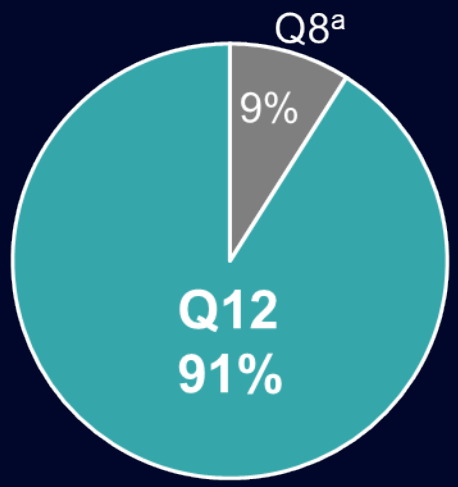
	LS mean change from baseline[b]	Difference in LS means vs aflibercept 2q8	Two-sided 95% CI	One-sided test for non-inferiority at four-letter margin
2q8	8.7	—	—	—
8q12	8.1	−0.57	−2.26, 1.13	p < 0.0001
8q16	7.2	−1.44	−3.27, 0.39	p = 0.0031

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

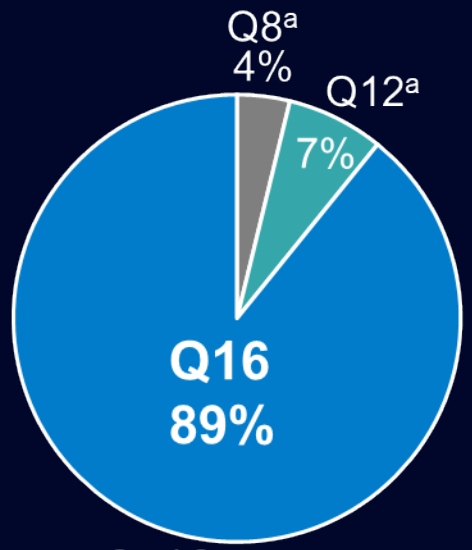
Proportion of 8 mg Patients Maintaining Q12- and Q16-Week Intervals Through Week 48

DME

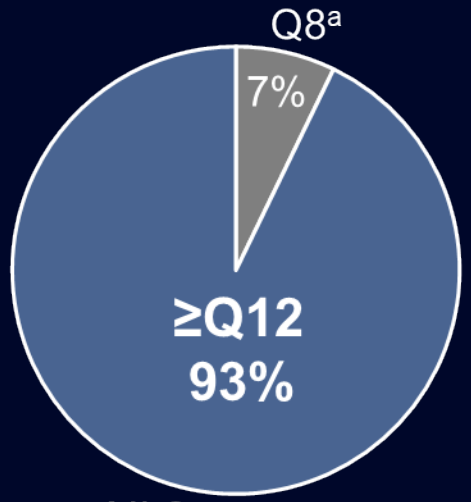
93% of 8 mg patients maintained dosing intervals ≥12 weeks



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

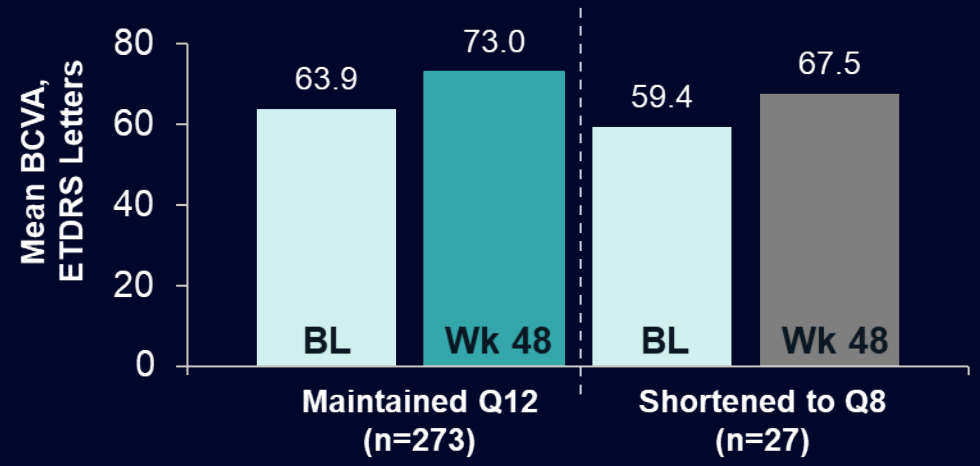
	8q12 (n=300)[a]		8q16 (n=156)[a]	
	Maintained	Shortened	Maintained	Shortened
n (%)	273 (91.0)	27 (9.0)	139 (89.1)	17 (10.9)
BCVA (ETDRS letters)	63.9 (10.1)	59.4 (10.0)	62.7 (11.2)	53.7 (12.8)
CRT (μm)	444.9 (129.8)	511.4 (117.5)	447.1 (112.5)	534.8 (134.3)
Baseline DRSS score (%)				
Level 43 or better	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

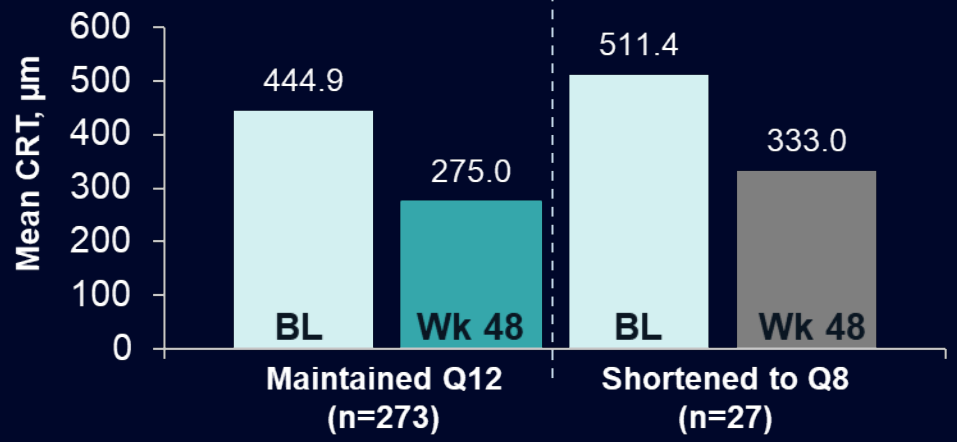
Compared with patients who maintained their randomized dosing intervals, those whose dosing intervals were shortened had on average **lower** BCVA and **greater** CRT at baseline

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

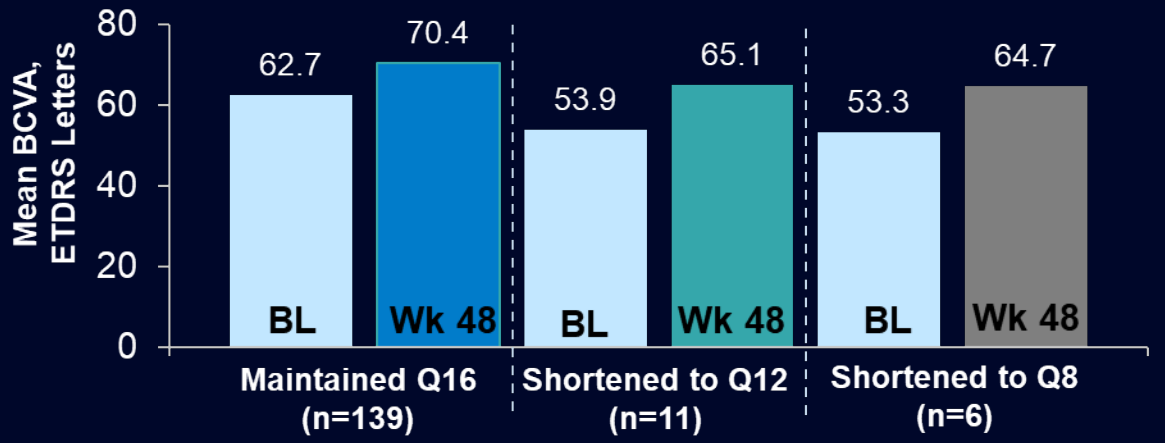
Absolute BCVA and CRT at Baseline and Week 48 by Dosing Interval

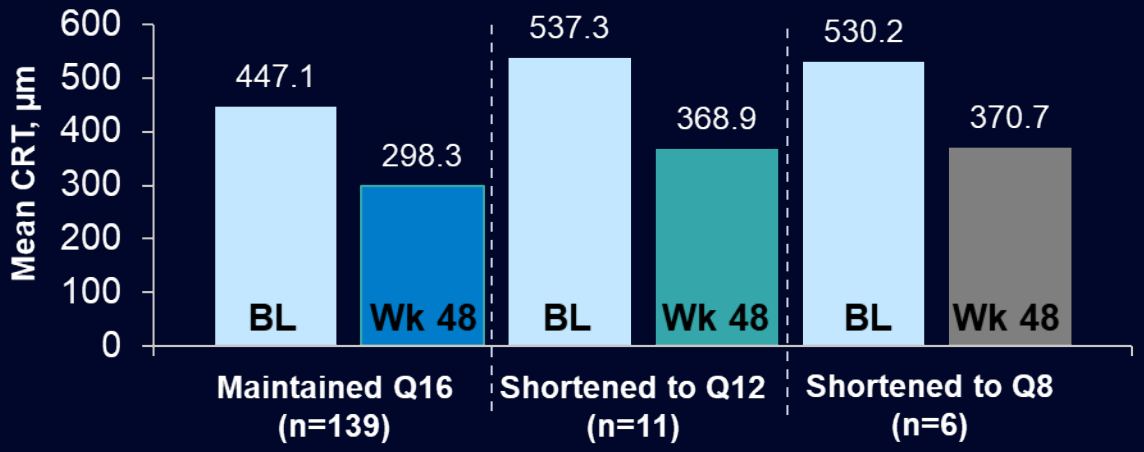
8q12 (n=300)[a]





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 CRT 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 CRT improvements at Week 48, although absolute BCVA and CRT values at Week 48 were not equivalent to those of patients with maintained dosing intervals