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Aflibercept 8 mg in DME: Key Results From the PHOTON Extension Study

Diana V. Do, MD,[1] on behalf of the PHOTON extension study investigators

[1]Byers Eye Institute, Stanford University School of Medicine, Palo Alto, CA, USA

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Disclosures

- Diana Do is a consultant to Allergan, AsclepiX, Boehringer Ingelheim, Clearside, Genentech, Kodiak Sciences, and Regeneron Pharmaceuticals, Inc.; and has received research funding from AsclepiX, Boehringer Ingelheim, Genentech, and Regeneron Pharmaceuticals, Inc.
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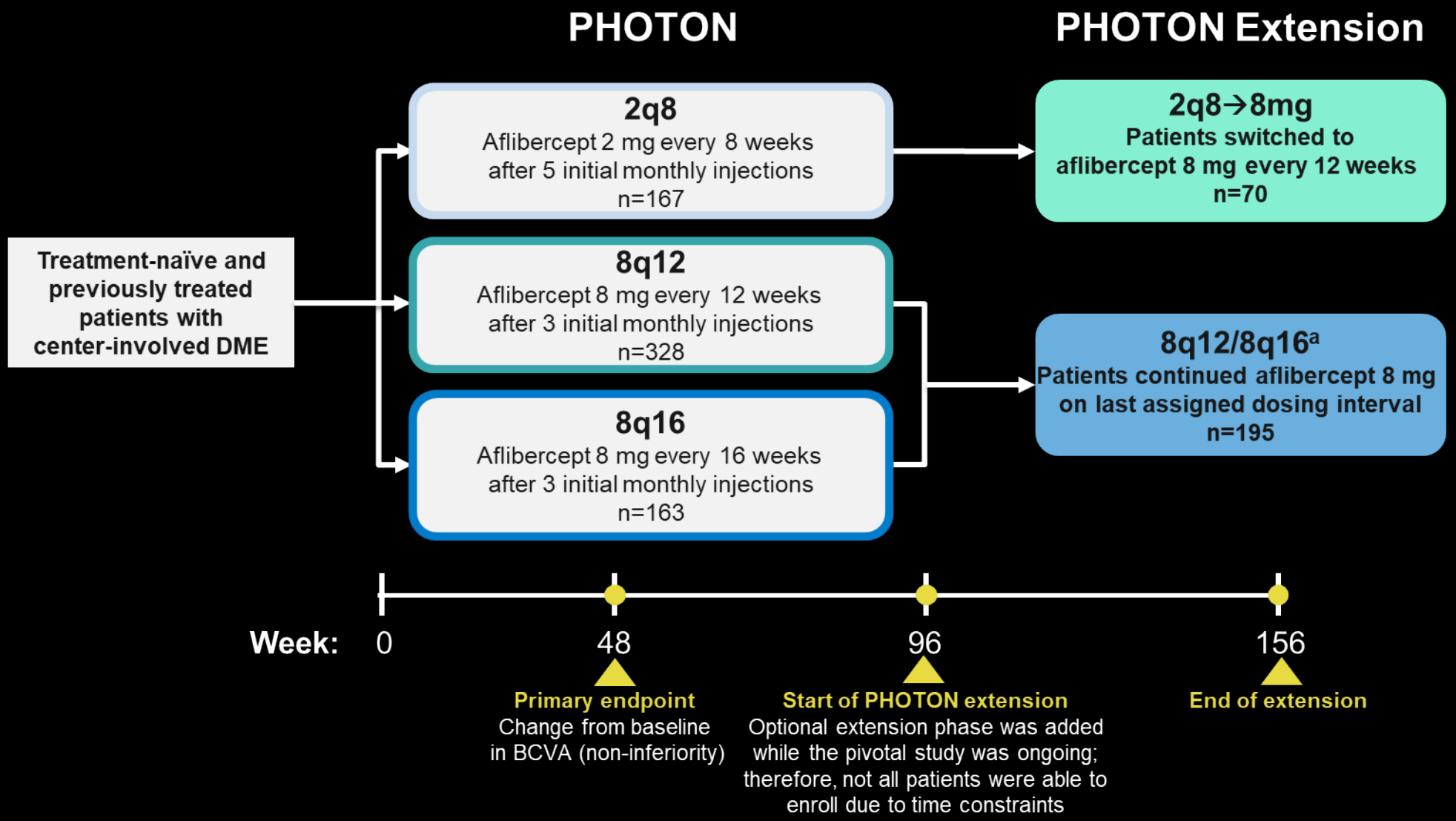
- Studies include research conducted on human patients. Institutional Review Board approval was obtained prior to initiation of the study

PHOTON Extension Study Design



[a]Patients who were randomized to the 8q12 or 8q16 groups at the beginning of the PHOTON study and continued treatment with aflibercept 8 mg through the PHOTON extension study.
BCVA, best-corrected visual acuity; DME, diabetic macular edema.

PHOTON Extension Study Design

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2q8→8mg n=70

8q12/8q16[a] n=195

- All patients received aflibercept 8 mg through Week 156
  - Patients who were treated with aflibercept 2q8 were switched to aflibercept 8 mg at Week 96 and immediately assigned to a 12-week dosing interval
- Mandatory visits were every 4 weeks through Week 108, then were quarterly through Week 156
- Dosing visits were scheduled as necessary based on individual dosing interval assignment

E-DRM: Interval Shortening During Year 3

- Patients were assessed at ***any visit*** beginning at Week 100
- **Criteria for interval shortening:**
  - >10-letter loss in BCVA from N-BL due to persistent or worsening DME **AND** >50-µm increase in CRT from N-BL
    OR
  - ≥15-letter loss from N-BL due to worsening DME
- Dosing intervals shortened by **2-week** increments
- Minimum interval was Q8

E-DRM: Interval Extension During Year 3

- Patients were assessed at ***dosing visits*** beginning at Week 100
- **Criteria for interval extension:**
  - <5-letter loss in BCVA from N-BL **AND**
  - CRT <300 µm (or <320 µm on Spectralis)
- Dosing intervals extended by **2-week** increments
- Maximum interval was Q24

[a]Patients who were randomized to the 8q12 or 8q16 groups at the beginning of the PHOTON study and continued treatment with aflibercept 8 mg through the PHOTON extension study.
N-BL defined as an average of values from Week 84, 88, and 92.
CRT, central retinal thickness; EOS, end of study; N-BL, new baseline.

Patient Disposition and Baseline Characteristics

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	PHOTON	PHOTON Extension		
	Total	2q8→8mg	8q12/8q16[a]	Total
Patients entering PHOTON study (FAS)	658	-	-	-
Patients entering PHOTON extension (eFAS)	-	70	195	265
Completion rate at Week 96 (%)	80.9	100	100	100
Completion rate at Week 156 (%)	-	82.9[b]	77.9[b]	79.2[b]
Age (years)	62.3 (10.4)	62.7 (8.5)	61.5 (11.3)	61.8 (10.7)
Female (%)	39.1	40.0	36.4	37.4
Race (%)				
White	71.6	65.7	77.4	74.3
Black or African American	9.4	8.6	6.7	7.2
Asian	15.3	21.4	14.4	16.2
Other[c]	3.7	4.3	1.5	2.3
Hemoglobin A1c (%)	8.0 (1.5)	8.2 (1.4)	7.9 (1.5)	8.0 (1.5)
History of hypertension (%)	78.1	70.0	77.4	75.5
BCVA (ETDRS letters)	62.5 (10.9)	61.6 (11.3)	62.8 (11.1)	62.5 (11.1)
CRT (μm)	454.0 (129.5)	472.3 (160.7)	460.2 (137.7)	463.4 (143.9)
Prior treatment for DME (%)	43.8	51.4	43.1	45.3

[a]Patients who were randomized to the 8q12 or 8q16 groups at the beginning of the PHOTON study and continued treatment with aflibercept 8 mg through the PHOTON extension study.
[b]Completion rate for PHOTON extension study based on eFAS. [c]Other includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, multiple races, and unreported race.
Data are mean (SD) unless otherwise indicated.
eFAS, PHOTON extension full analysis set; ETDRS, Early Treatment Diabetic Retinopathy Study; FAS, full analysis set.

Mean BCVA Through Week 156

All Patients in PHOTON Extension

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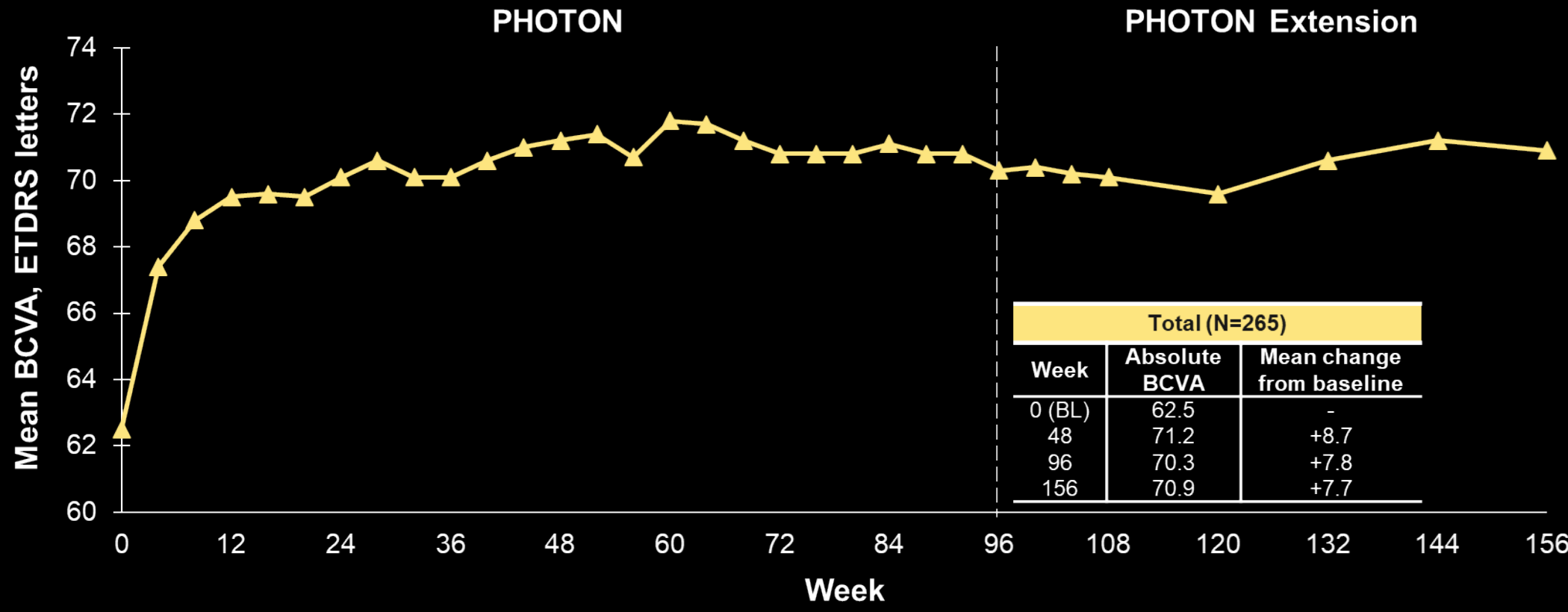

Total (N=265)		
Week	Absolute BCVA	Mean change from baseline
0 (BL)	62.5	-
48	71.2	+8.7
96	70.3	+7.8
156	70.9	+7.7

eFAS, observed cases.

Mean BCVA[a] Through Week 156

2q8→8mg and 8q12/8q16[b] Patients

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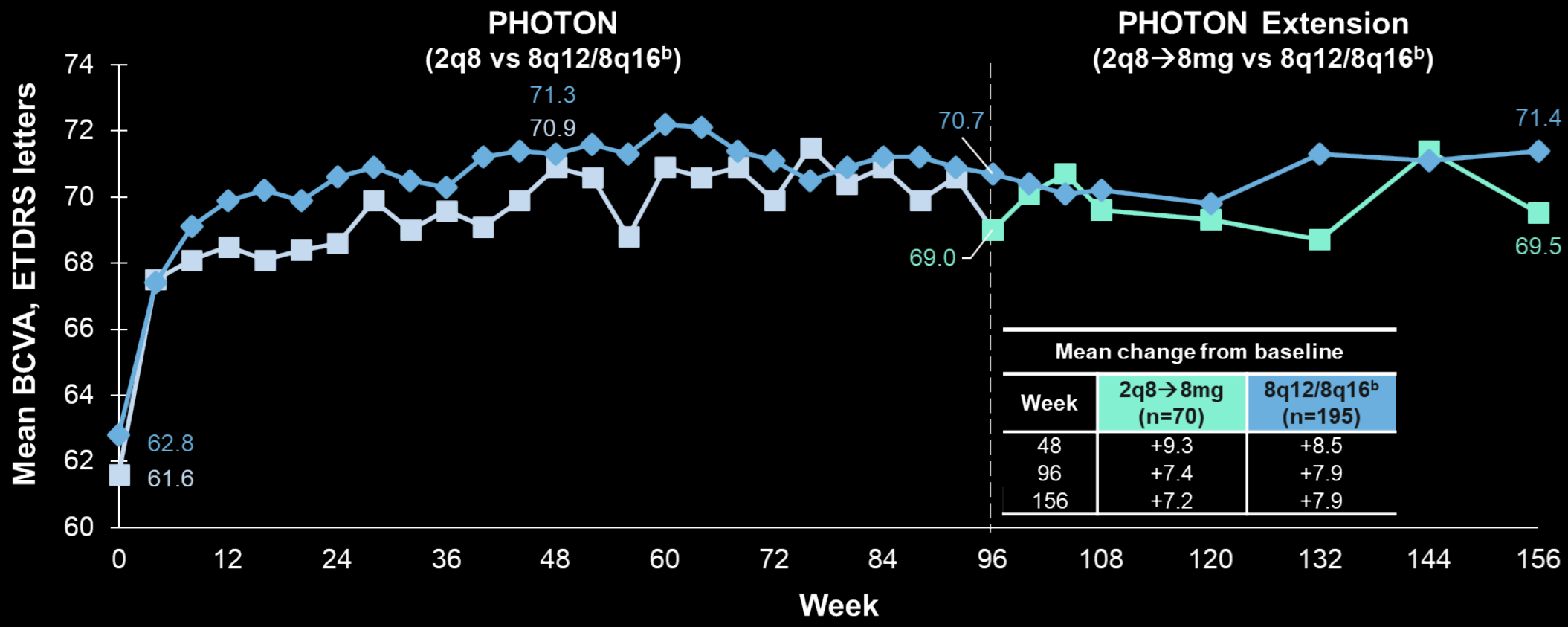


Mean change from baseline		
Week	2q8→8mg (n=70)	8q12/8q16[b] (n=195)
48	+9.3	+8.5
96	+7.4	+7.9
156	+7.2	+7.9

Mean number of injections from baseline to Week 96[c]

2q8: 13.8

8q12/8q16[b]: 8.9

Mean number of injections from Week 96 to Week 156[c]

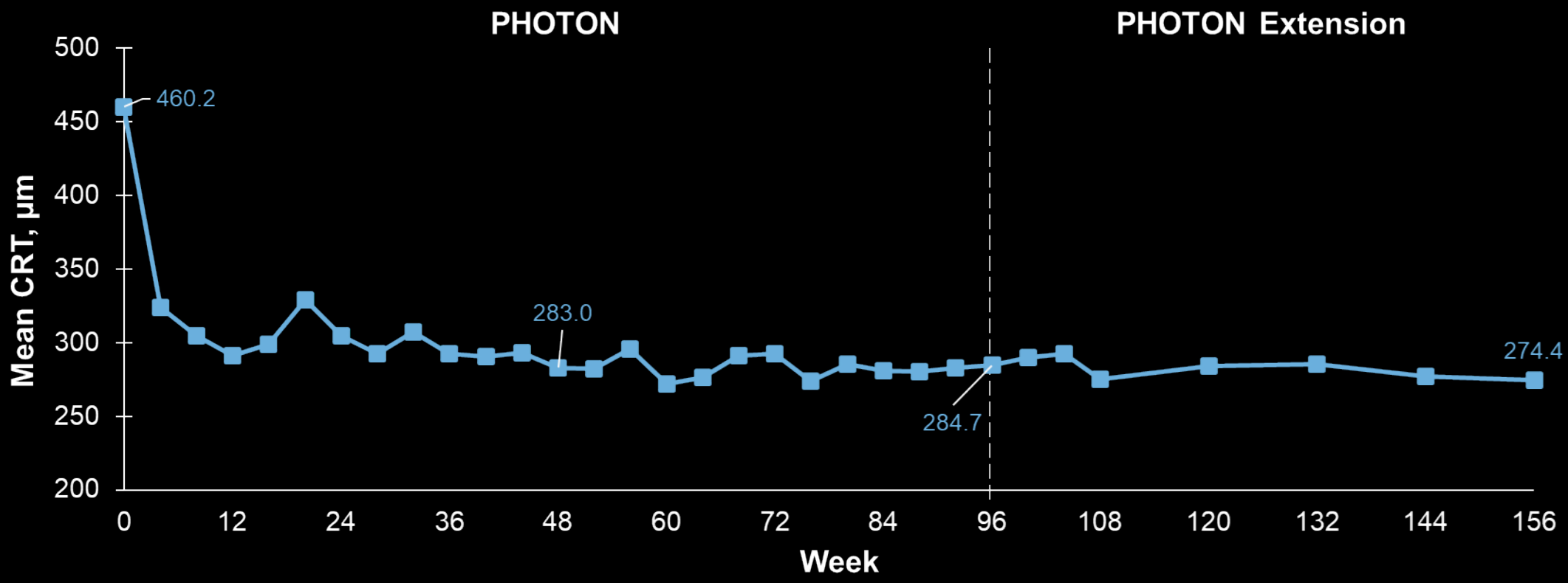
2q8→8mg: 4.4

8q12/8q16[b]: 3.3

[a]eFAS, observed cases.
[b]Patients who were randomized to the 8q12 or 8q16 groups at the beginning of the PHOTON study and continued treatment with aflibercept 8 mg through the PHOTON extension study.
[c]eFAS.

Mean CRT Through Week 156

All 8q12/8q16[a] Patients

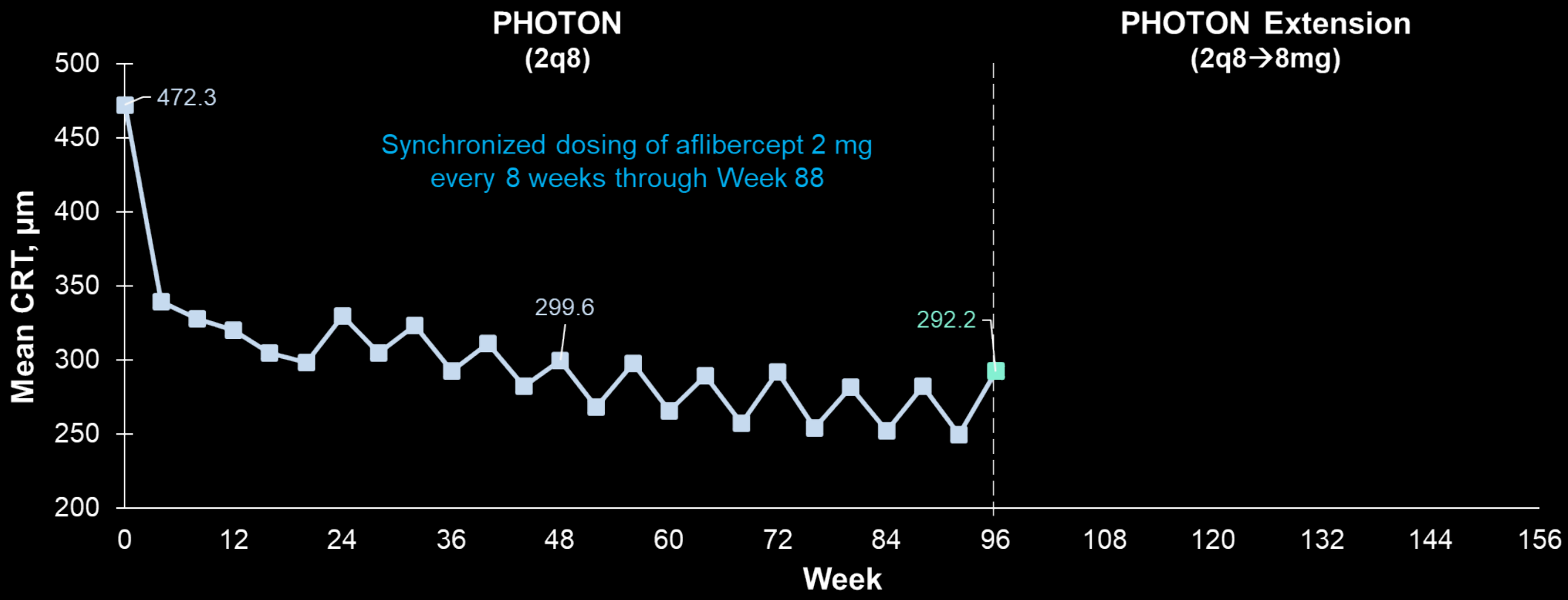


	Mean change from baseline (µm)		
	Week 48	Week 96	Week 156
8q12/8q16[a] (n=195)	-177.6	-176.0	-187.9

[a]Patients who were randomized to the 8q12 or 8q16 groups at the beginning of the PHOTON study and continued treatment with aflibercept 8 mg through the PHOTON extension study.
eFAS, observed cases.

Mean CRT Through Week 156

2q8→8mg Patients

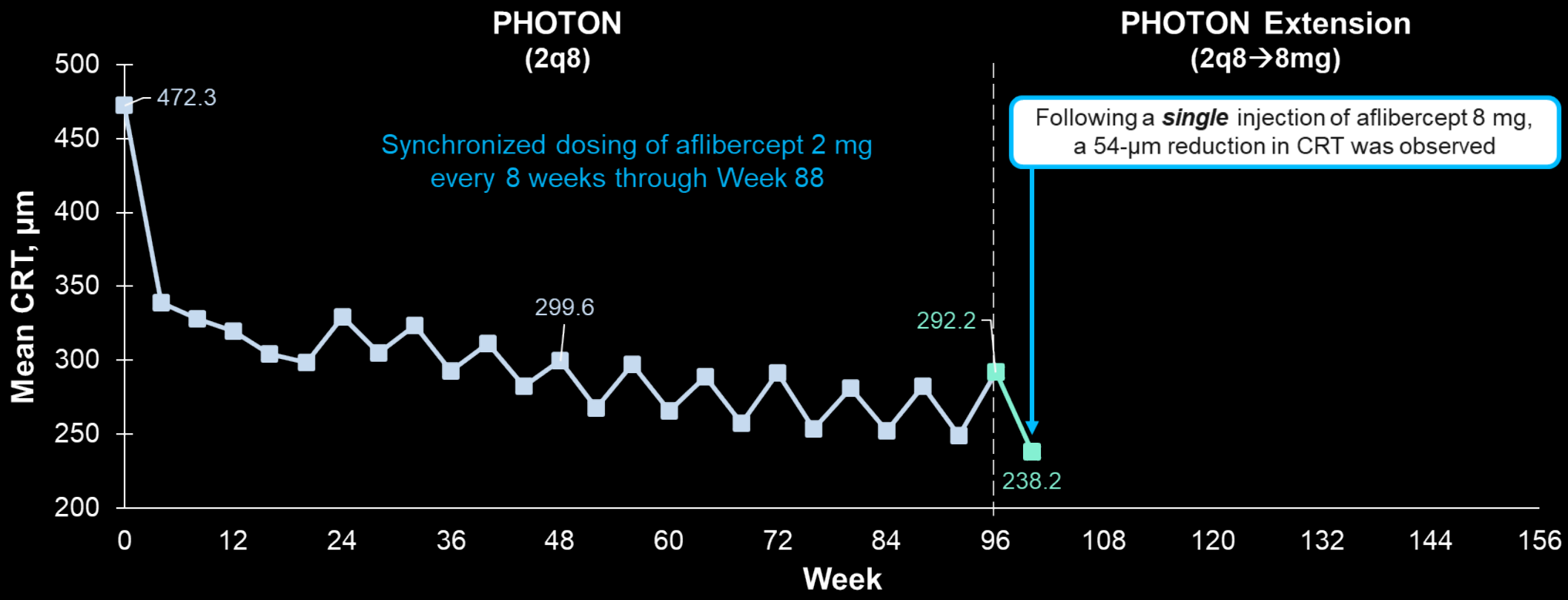


	Mean change from baseline (µm)	
	Week 48	Week 96
2q8→8mg (n=70)	-172.7	-181.9

eFAS, observed cases.

Mean CRT Through Week 156

2q8→8mg Patients



	Mean change from baseline (µm)	
	Week 48	Week 96
2q8→8mg (n=70)	-172.7	-181.9

eFAS, observed cases.

Mean CRT Through Week 156

2q8→8mg Patients

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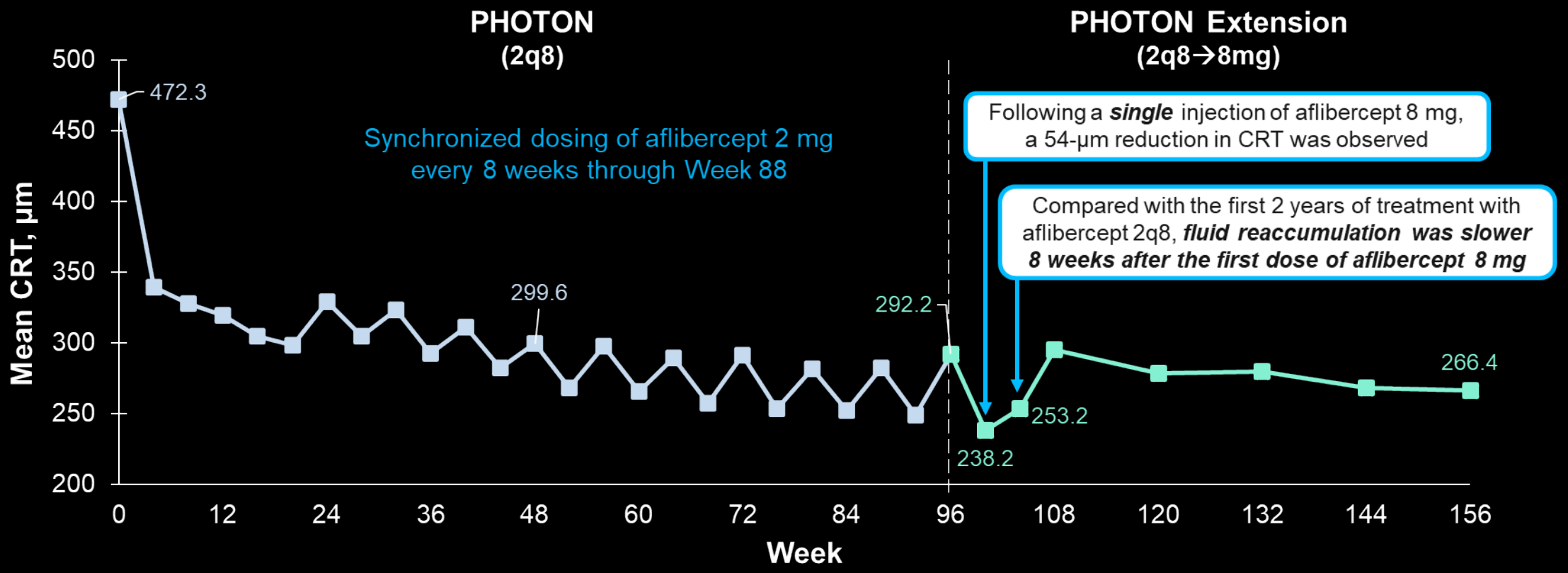

	Mean change from baseline (µm)		
	Week 48	Week 96	Week 156
2q8→8mg (n=70)	-172.7	-181.9	-210.4

Numerically greater reduction in CRT was observed at Week 156 after switching to aflibercept 8 mg compared with aflibercept 2q8

eFAS, observed cases.

Majority of Aflibercept 8 mg-treated Patients Achieved Extended Dosing Intervals at Week 156

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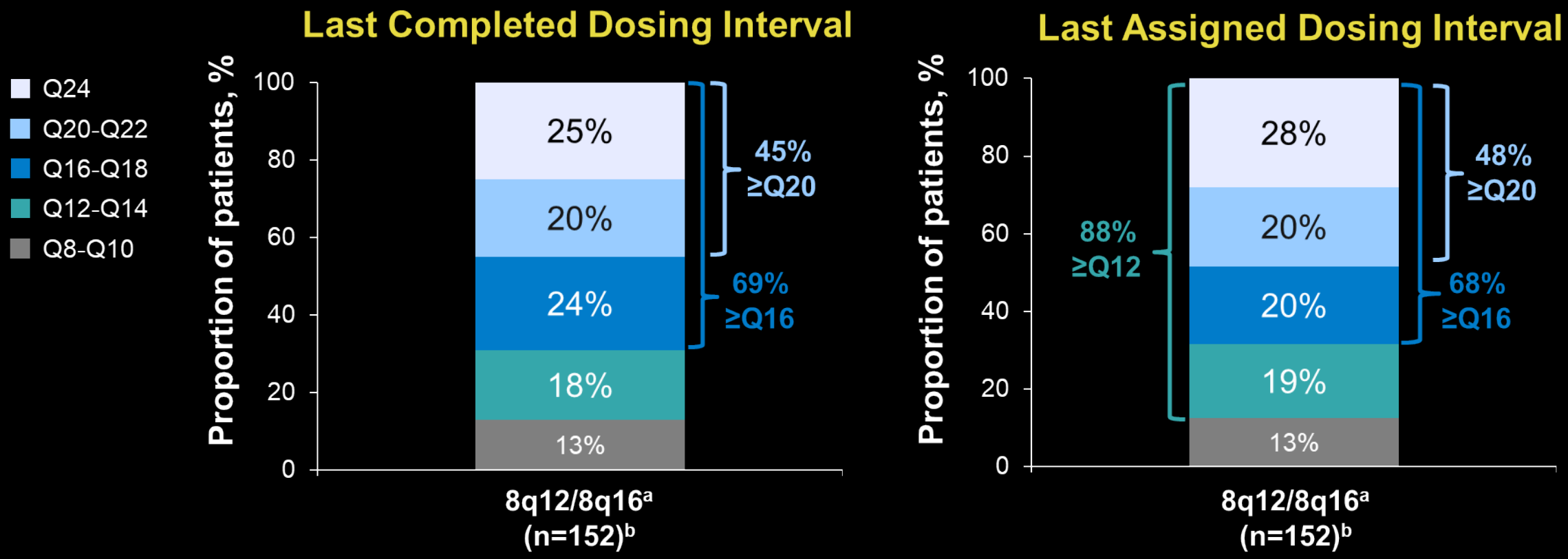

2q8→8mg group:

83% of patients had a last assigned dosing interval of ≥12 weeks at Week 156

[a]Patients who were randomized to the 8q12 or 8q16 groups at the beginning of the PHOTON study and continued treatment with aflibercept 8 mg through the PHOTON extension study.
[b]eFAS, patients completing Week 156.
Values may not add up to 100% due to rounding.

Ocular Safety Through Week 156[a]

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	2q8→8mg	8q12/8q16[b]	Total
N (eSAF)	70	195	265
Ocular TEAEs, n (%)	37 (52.9)	108 (55.4)	145 (54.7)
Ocular SAEs, n (%)	3 (4.3)	4 (2.1)	7 (2.6)
Intraocular inflammation, n (%)	1 (1.4)	3 (1.5)	4 (1.5)
Iritis	0	2 (1.0)	2 (0.8)
Iridocyclitis	1 (1.4)	0	1 (0.4)
Uveitis	1 (1.4)	0	1 (0.4)
Endophthalmitis	0	1 (0.5)	1 (0.4)

- Ocular TEAEs reported in >4% of all patients included cataract, vitreous floaters, vitreous detachment, and diabetic retinal edema
- No cases of occlusive vasculitis were reported

[a]Cumulative events in the study eye from baseline through Week 156.
[b]Patients who were randomized to the 8q12 or 8q16 groups at the beginning of the PHOTON study and continued treatment with aflibercept 8 mg through the PHOTON extension study.
SAE, serious adverse event; eSAF, PHOTON extension safety analysis set; TEAE, treatment-emergent adverse event.

Non-ocular Safety Through Week 156

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	2q8→8mg	8q12/8q16[a]	Total
N (eSAF)	70	195	265
Non-ocular SAEs, n (%)	24 (34.3)	58 (29.7)	82 (30.9)
APTC events, n (%)	5 (7.1)	14 (7.2)	19 (7.2)
Deaths, n (%)	2 (2.9)	10 (5.1)	12 (4.5)

[a]Patients who were randomized to the 8q12 or 8q16 groups at the beginning of the PHOTON study and continued treatment with aflibercept 8 mg through the PHOTON extension study.
APTC, Anti-Platelet Trialists' Collaboration.

PHOTON Extension: Key Week 156 Results

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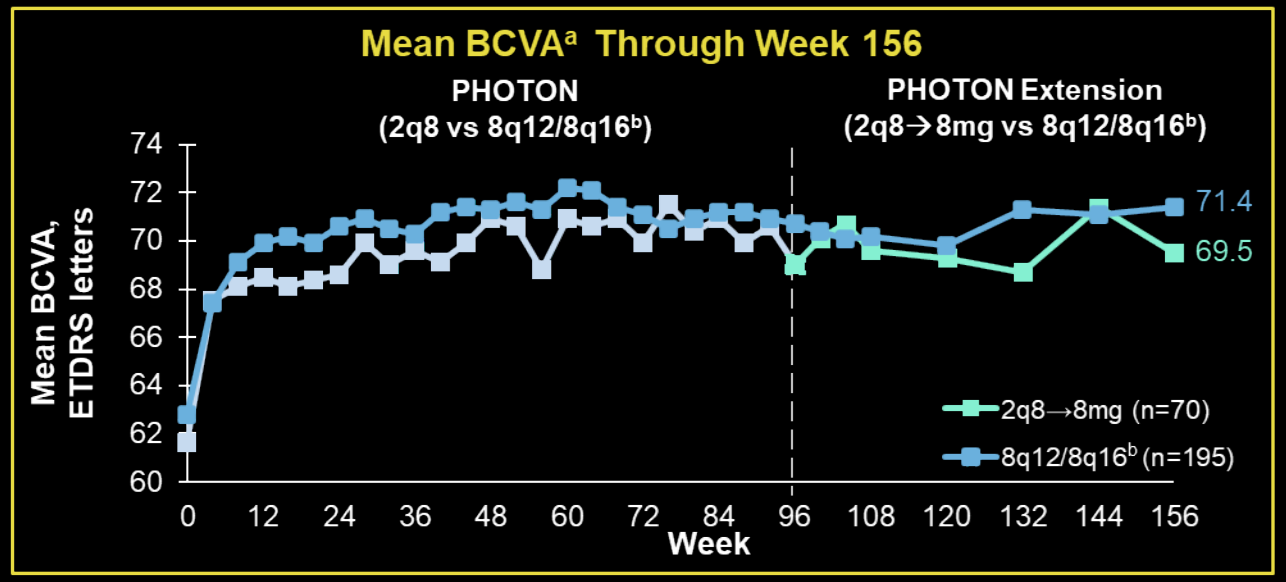
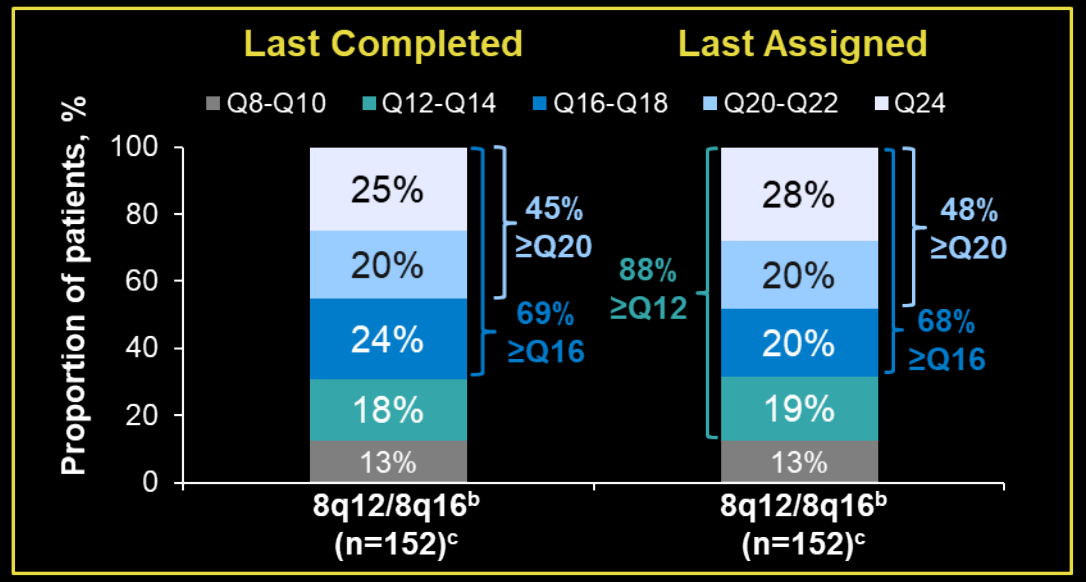
- Patients in the **8q12/8q16 group** maintained visual and anatomic improvements achieved in the first 2 years, with the majority of patients on extended dosing intervals
  - 45% completed ≥20-week dosing intervals and 48% had a last assigned dosing interval of ≥20 weeks at Week 156
- In the **2q8→8mg group**, visual and anatomic improvements achieved with fixed 2q8 dosing were maintained with aflibercept 8 mg
  - 83% of patients achieved ≥12-week dosing intervals at Week 156
  - ***Longer duration of action with aflibercept 8 mg*** vs 2 mg was ***further supported*** by ***slower fluid reaccumulation*** following the first aflibercept 8-mg injection
- No new safety signals were reported with aflibercept 8 mg through Week 156





[a]eFAS, observed cases.
[b]Patients who were randomized to the 8q12 or 8q16 groups at the beginning of the PHOTON study and continued treatment with aflibercept 8 mg through the PHOTON extension study.
[c]eFAS, patients completing Week 156.