Week 96 Outcomes in Aflibercept 8 mg– and 2 mg–Treated Patients by Prior DME Treatment Status: a Subgroup Analysis of the Phase 2/3 PHOTON Trial

Manjot K Gill, MD, MS, FRCS(C), on behalf of the *PHOTON* study investigators
Northwestern University Feinberg School of Medicine, Chicago, Illinois

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Note: This slide for review purposes only. To be removed prior to submission as ARVO guidelines indicate they will provide a disclosure slide

Disclosures

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- Study disclosures: This study includes research conducted on human patients. Institutional review board approval was obtained prior to study initiation
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Background

- Aflibercept 8 mg is a novel intravitreal formulation that delivers a 4-times higher molar dose than aflibercept 2 mg, potentially extending VEGF suppression over a longer period
- 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]
  - Given that approximately 44% of patients in PHOTON received prior treatment for DME,[a] there is an opportunity to assess treatment outcomes in patients with prior DME treatment

This subgroup analysis evaluated visual acuity and anatomic outcomes (CRT and DRSS) in PHOTON patients by prior DME treatment status

[a]Previous treatments for DME were laser, intravitreal anti-VEGF therapy, and corticosteroids.
BCVA, best-corrected visual acuity; CRT, central retinal thickness; DME, diabetic macular edema; DRSS, Diabetic Retinopathy Severity Scale; VEGF, vascular endothelial growth factor.

PHOTON Study Design

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

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 (non-inferiority)

↓

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

[a]Treatment-naive and previously treated patients.
2q8, 2 mg every 8 weeks after 5 initial monthly injections; 8q12, 8 mg every 12 weeks after 3 initial monthly injections; 8q16, 8 mg every 16 weeks after 3 initial monthly injections.

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.

Baseline Demographics

	With Prior DME Treatment			Without Prior DME Treatment		
	2q8 (n=74)	8q12 (n=146)	8q16 (n=71)	2q8 (n=93)	8q12 (n=182)	8q16 (n=92)
Age, years	64.4 (8.9)	62.7 (10.9)	63.0 (8.4)	62.0 (10.4)	61.6 (11.3)	60.9 (10.3)
Female, %	45.9	39.7	40.8	44.1	33.0	38.0
Race, %						
White	64.9	69.2	77.5	68.8	71.4	79.3
Asian	21.6	19.9	18.3	15.1	10.4	10.9
Black or African American	9.5	7.5	4.2	11.8	13.2	6.5
American Indian or Alaskan Native	0.0	0.7	0.0	0.0	0.5	0.0
Other	2.7	1.4	0.0	2.2	2.2	1.1
Not reported	1.4	1.4	0.0	2.2	1.1	2.2
Hispanic or Latino, %	18.9	17.1	22.5	18.3	15.9	19.6
Duration of diabetes, years	16.7 (10.6)	16.2 (9.4)	16.6 (9.7)	15.5 (9.6)	14.5 (10.3)	15.0 (11.4)

Data are mean (SD) unless otherwise indicated.

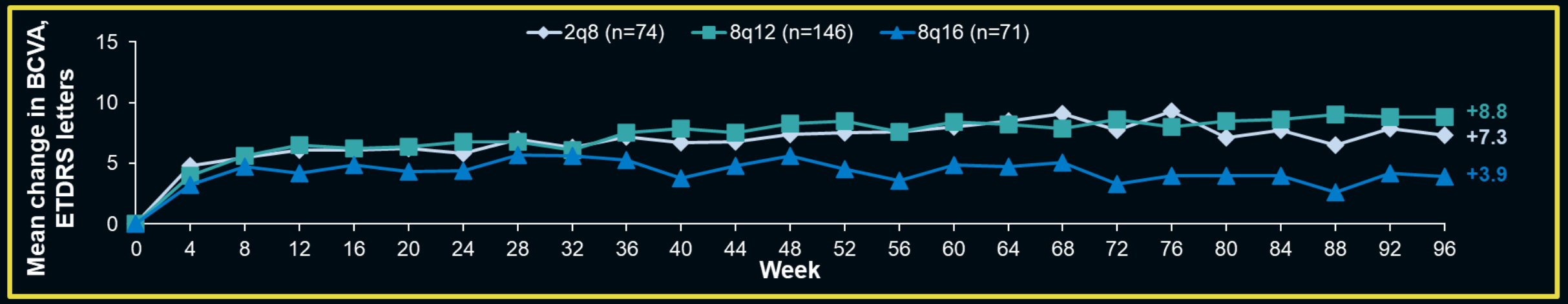
Baseline Ocular Characteristics

	With Prior DME Treatment			Without Prior DME Treatment		
	2q8 (n=74)	8q12 (n=146)	8q16 (n=71)	2q8 (n=93)	8q12 (n=182)	8q16 (n=92)
BCVA, ETDRS letters	62.1 (10.9)	62.2 (10.7)	58.6 (11.9)	61.0 (11.5)	64.8 (9.5)	63.7 (11.2)
Snellen equivalent, %						
20/32 (>73 to 78 letters)	14.9	16.4	5.6	9.7	19.2	20.7
20/40 or worse (≤73 letters)	85.1	83.4	94.4	90.3	80.8	79.3
CRT, µm	472.7 (162.3)	456.9 (123.9)	460.6 (109.3)	444.9 (127.1)	442.9 (130.2)	460.1 (124.7)
DRSS categories, %						
Better or equal to level 43	70.3	66.4	67.6	57.0	54.9	64.1
Level 47 or worse	25.7	28.1	23.9	36.6	39.6	31.5
Missing/ungradable	4.1	5.5	8.5	6.5	5.5	4.3

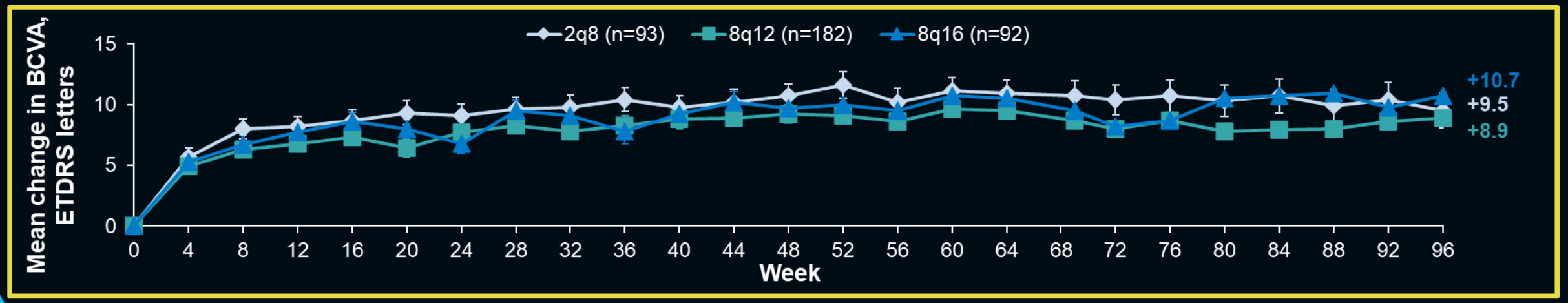
Data are mean (SD) unless otherwise indicated.
ETDRS, Early Treatment Diabetic Retinopathy Study.

Mean Change in BCVA Through Week 96

With Prior DME Treatment



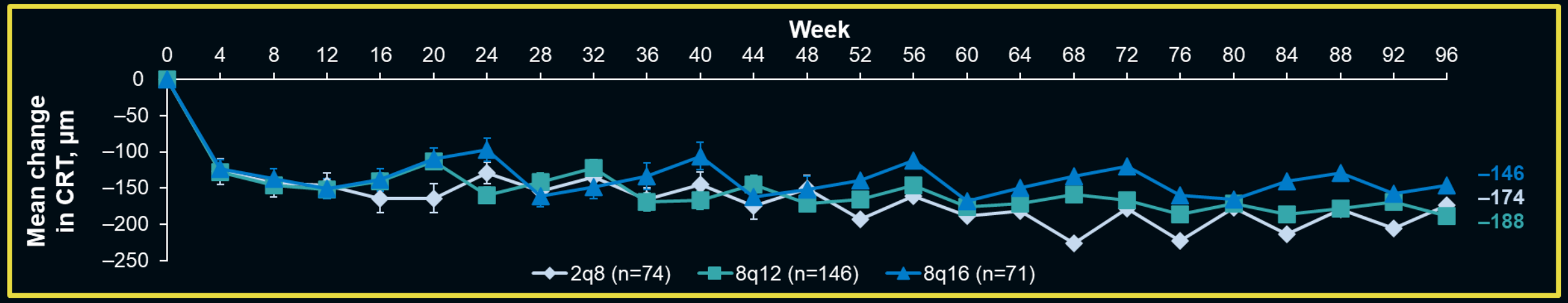
Without Prior DME Treatment



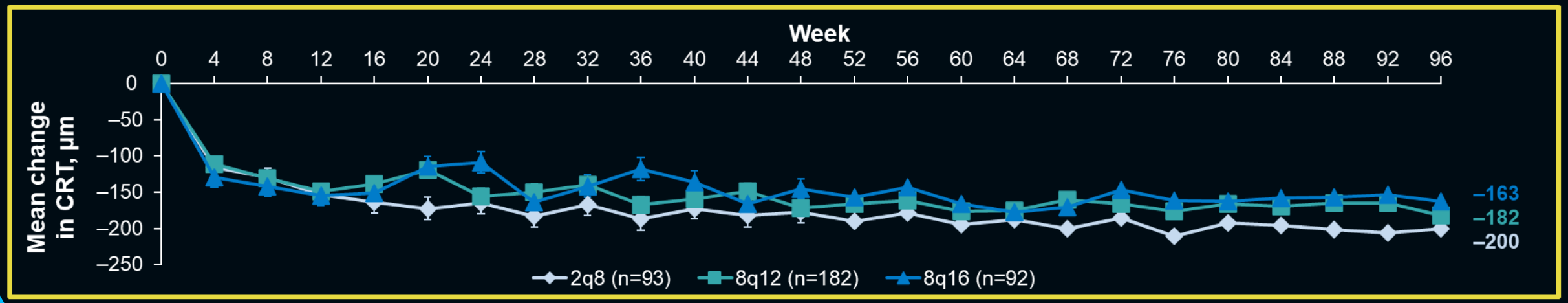
FAS, observed cases (censoring data post-intercurrent event).
FAS, full analysis set.

Mean Change in CRT Through Week 96

With Prior DME Treatment



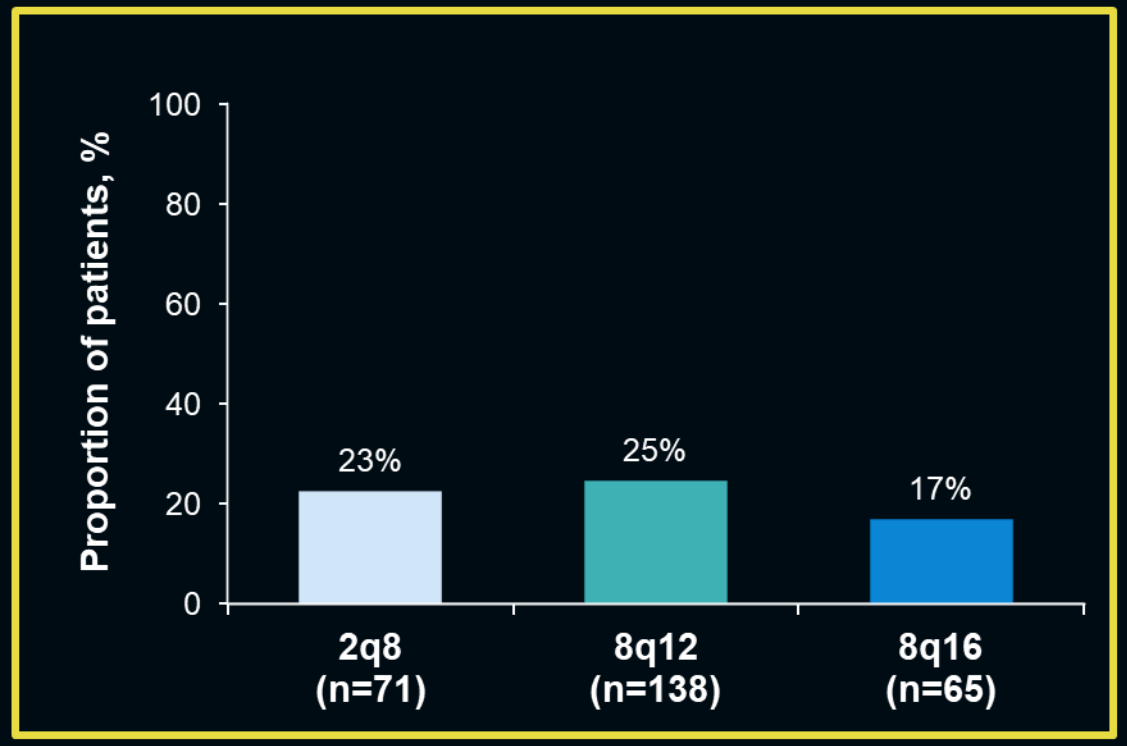
Without Prior DME Treatment



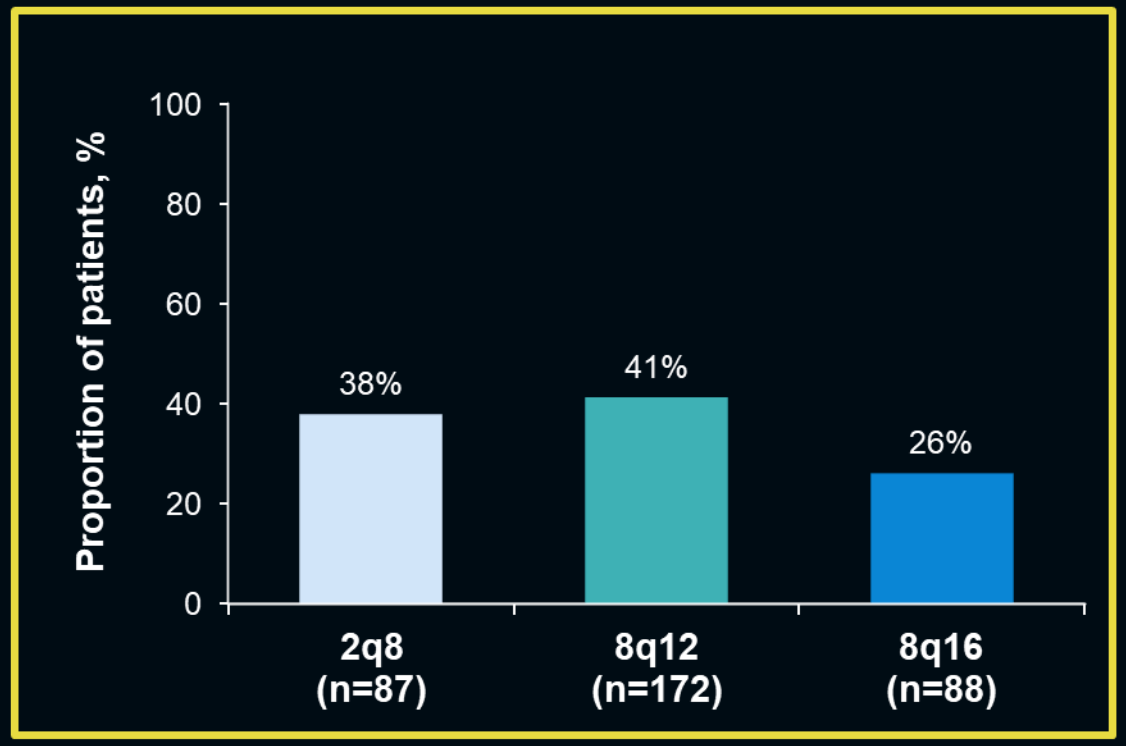
FAS, observed cases (censoring data post-intercurrent event).

Proportion of Patients With ≥2-Step DRSS Improvement From Baseline at Week 96

With Prior DME Treatment



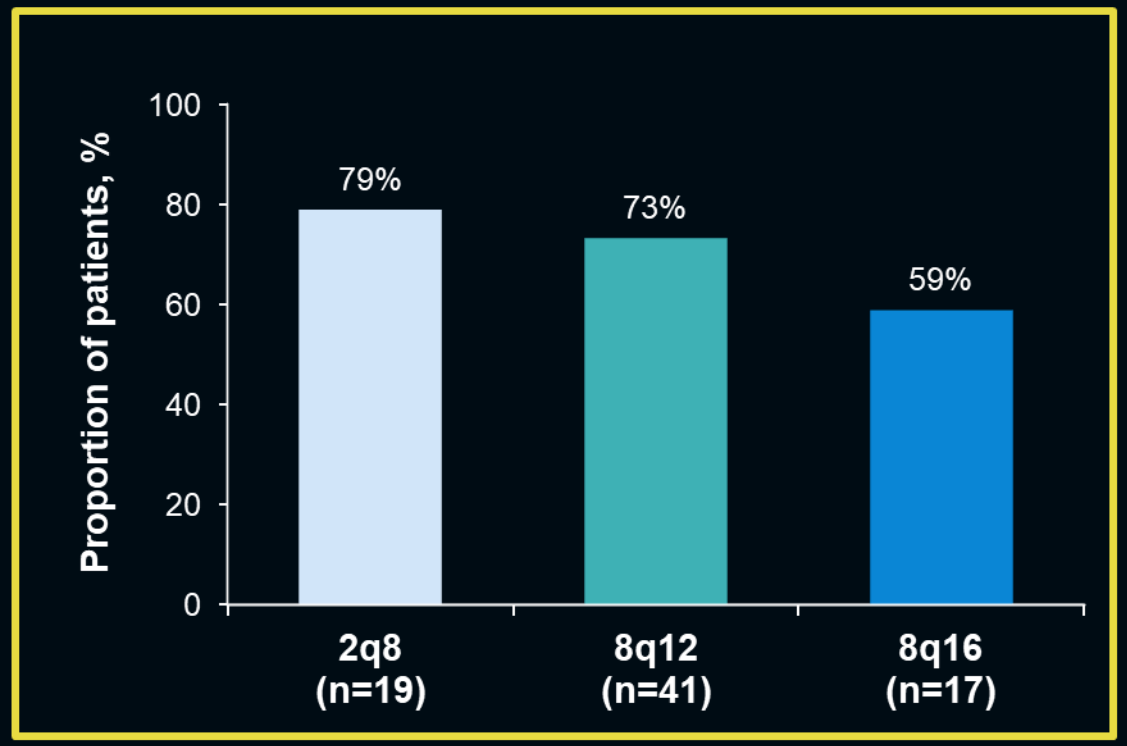
Without Prior DME Treatment



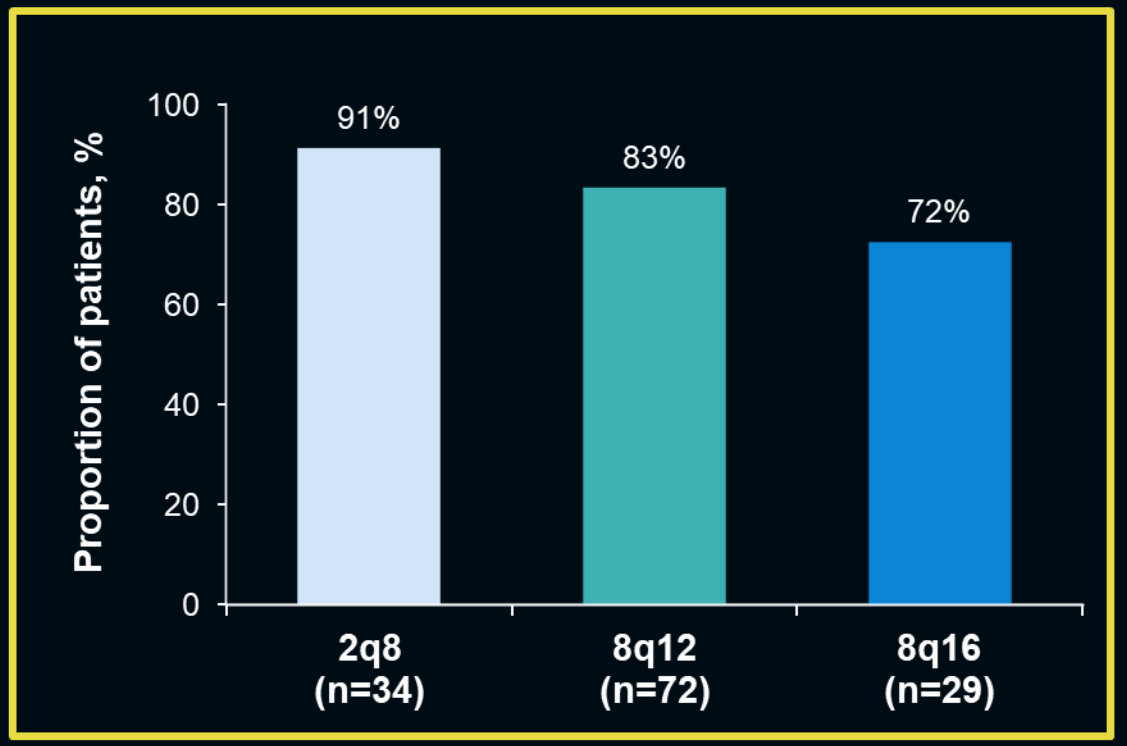
FAS, LOCF.
LOCF, last observation carried forward.

Proportion of Patients With Baseline DRSS 47 or Worse and ≥2-Step DRSS Improvement from Baseline at Week 96

With Prior DME Treatment

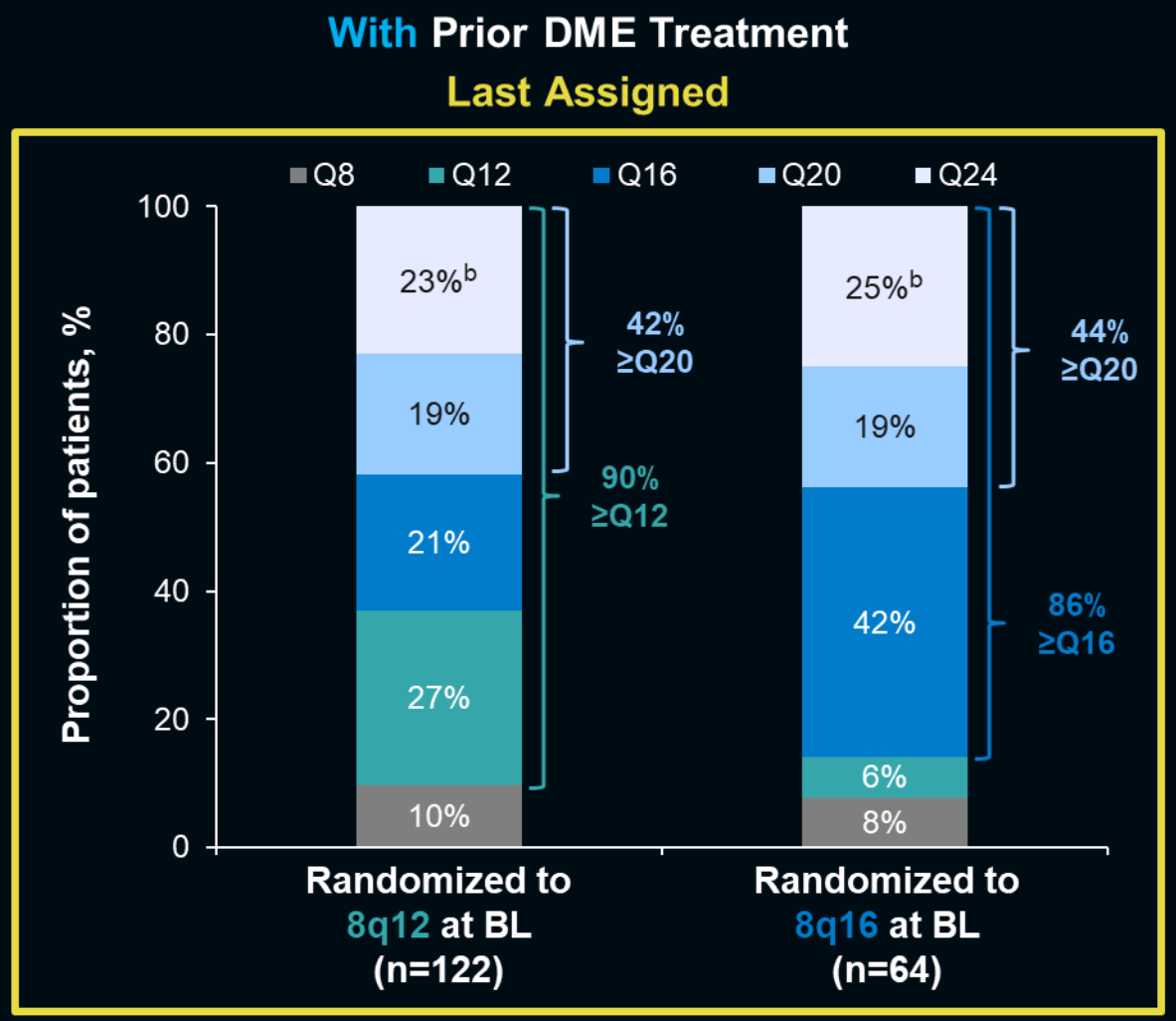


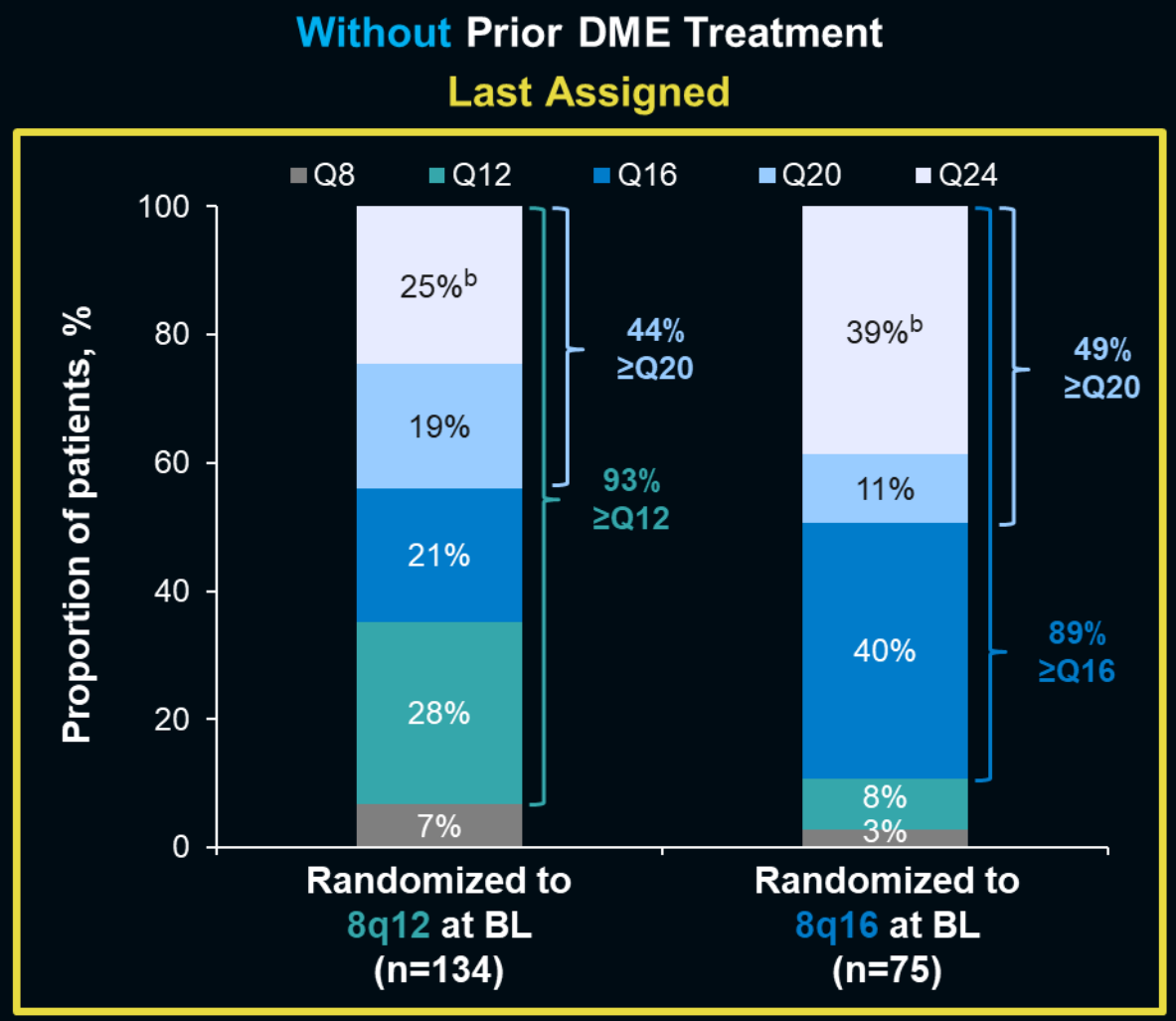
Without Prior DME Treatment



FAS, LOCF.

Large Proportion of Patients Qualified for Interval Extension in Year 2[a]





FAS, patients who completed Week 96 visit. Values may not add up to 100% due to rounding.
[a]Dosing intervals were extended in Year 2 if patients had <5-letter loss in BCVA from Week 12 and CRT <300 µm (or <320 µm on Spectralis). [b]Patients were assigned to 24-week dosing intervals if they continued to meet extension criteria but there was not sufficient time to complete the interval within the 96-week study period.
BL, baseline; Q12, every 12 weeks; Q16, every 16 weeks; Q20, every 20 weeks.

Conclusions

- In patients with prior DME treatment, mean BCVA gain at Week 96 was numerically greater with 2q8 and 8q12 compared with 8q16, suggesting that some patients in this subgroup could have benefited from more frequent treatment
  - This may have been a particularly recalcitrant subgroup as the baseline VA in this group was lower than the other subgroups
- CRT improvements were generally comparable at Week 96 irrespective of prior DME treatment status
- Proportions of patients with ≥2-step improvement in DRSS score at Week 96 trended numerically higher across all treatment groups in patients without versus with prior DME treatment
- Similar proportions of patients in the aflibercept 8q12 and 8q16 groups had a last assigned dosing interval of ≥20 weeks at Week 96 irrespective of prior DME treatment status