Week 48 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

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Disclosures

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- Dr. Moshfeghi has served as a consultant for Allergan, Alimera, Annexon, Apellis, Genentech/Roche, Novartis, Ocular Therapeutix, OcuTerra, Pr3vent, Regeneron Pharmaceuticals, Inc., SciNeuro, Valitor, and Waldo dba Ainsly Ltd.; has received research funding from Genentech/Roche, Novartis, and Regeneron Pharmaceuticals, Inc.; and has been a stockholder of Ocular Therapeutix, Placid0, Pr3vent, Waldo dba Ainsly Ltd., and Valitor
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- Study disclosures: This study includes research conducted on human patients. Institutional Review Board approval was obtained prior to study initiation

Background

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- 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 of time
- 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 48[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 of the PHOTON trial evaluated visual and anatomic outcomes in patients by prior DME treatment status

[a]Prior DME treatment status was categorized as yes/no in the EDC. Previous treatments for DME were laser, intravitreal anti-VEGF therapy, and corticosteroids.
BCVA, best-corrected visual acuity; DME, diabetic macular edema; EDC, electronic data capture record; VEGF, vascular endothelial growth factor.
1. Brown DM. Intravitreal aflibercept injection 8 mg for DME: results from the phase 2/3 PHOTON trial. Presented at: American Academy of Ophthalmology; September 30, 2022; Chicago, IL.

PHOTON Study Design

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Multi-center, randomized, double-masked study in patients with DME[a]
Randomized 1 (2q8) : 2 (8q12) : 1 (8q16)
Note: 2 mg arm received 5 initial monthly injections versus 8 mg arms, which received only 3 initial monthly injections

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

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

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

[a]Treatment naïve and previously treated.
DRSS, Diabetic Retinopathy Severity Scale.

PHOTON: Dose Regimen Modifications in Year 1

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Primary Endpoint

	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	X	X	X	X	X	o	X	o	X	o	X	o	X
8q12	X	X	X	o	o	X	o	o	X	o	o	X	o
8q16	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 CRT

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 injections. Note: Figure does not reflect all dosing options once a patient is shortened.
[a]All assessments compared to Week 12.
CRT, central retinal thickness; DRM, dose regimen modification.

Baseline Demographics

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	With Prior DME Treatment			Without Prior DME Treatment		
	2q8 (n=74)	8q12 (n=143)	8q16 (n=71)	2q8 (n=93)	8q12 (n=185)	8q16 (n=92)
Age, years	64.4 (8.9)	62.8 (11.0)	63.0 (8.4)	62.0 (10.4)	61.6 (11.3)	60.9 (10.3)
Female, %	45.9	39.2	40.8	44.1	33.5	38.0
Race, %						
White	64.9	69.9	77.5	68.8	70.8	79.3
Asian	21.6	19.6	18.3	15.1	10.8	10.9
Black or African American	9.5	7.0	4.2	11.8	13.5	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	17.5	22.5	18.3	15.7	19.6
Duration of diabetes, years	16.7 (10.6)	16.0 (9.4)	16.6 (9.7)	15.3 (9.6)	14.5 (10.3)	15.0 (11.4)

Data are mean (SD) unless otherwise indicated.

Baseline Ocular Characteristics

DME

	With Prior DME Treatment			Without Prior DME Treatment		
	2q8 (n=74)	8q12 (n=143)	8q16 (n=71)	2q8 (n=93)	8q12 (n=185)	8q16 (n=92)
BCVA, ETDRS letters	62.1 (10.9)	62.3 (10.5)	58.6 (11.9)	61.0 (11.5)	64.7 (9.7)	63.7 (11.2)
Snellen equivalent, %						
20/32 (>73 to 78 letters)	14.9	16.8	5.6	9.7	18.4	20.7
20/40 or worse (≤73 letters)	85.1	83.2	94.4	90.3	81.1	79.3
CRT, µm	472.7 (162.3)	455.7 (124.0)	460.6 (109.3)	444.9 (127.1)	444.1 (130.1)	460.1 (124.7)
DRSS categories, %						
Better or equal to level 43	70.3	66.4	67.6	57.0	55.1	64.1
Level 47 or worse	25.7	28.0	23.9	36.6	39.5	31.5
Missing/ungradable	4.1	5.6	8.5	6.5	5.4	4.3

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

Mean Change in BCVA Through Week 48

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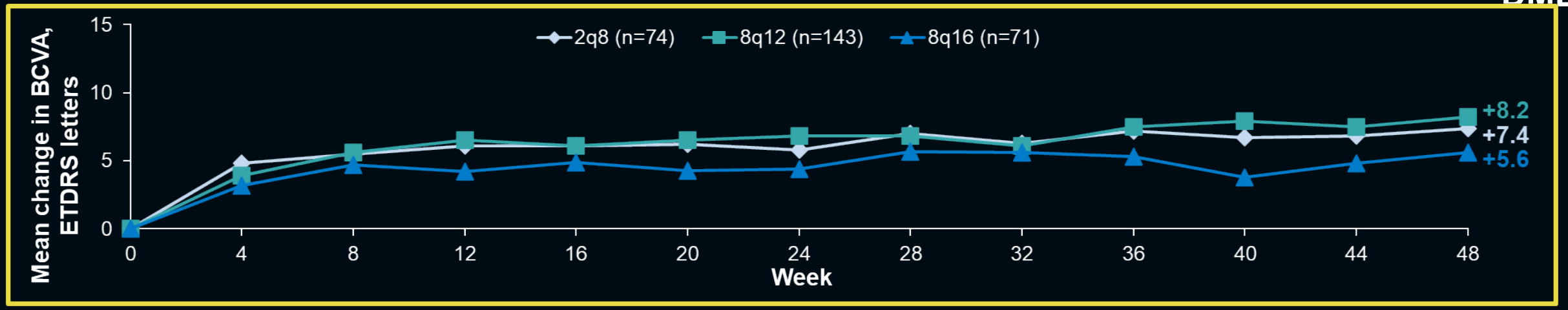
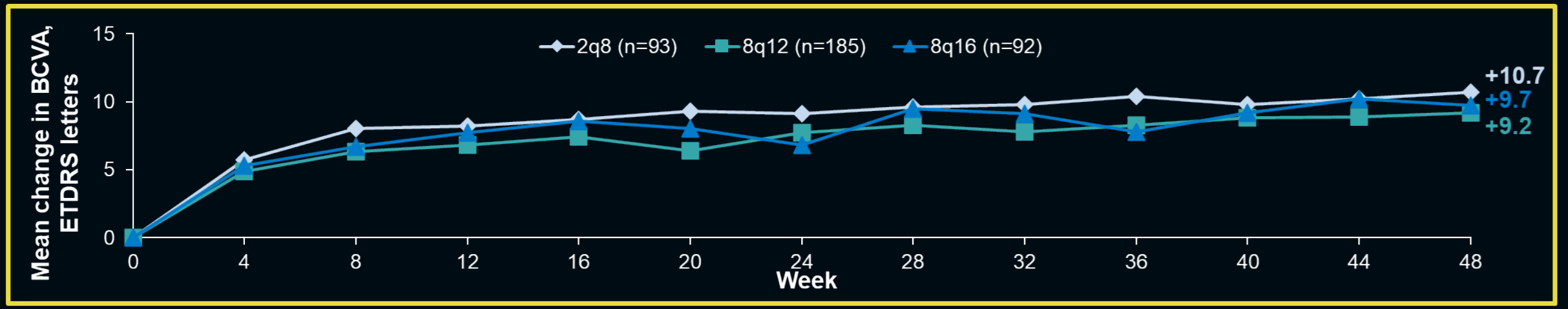
DME

With Prior DME Treatment



Without Prior DME Treatment



FAS, observed cases.
FAS, full analysis set.

Proportion of Patients With ≥2-step DRSS Improvement From Baseline at Week 48

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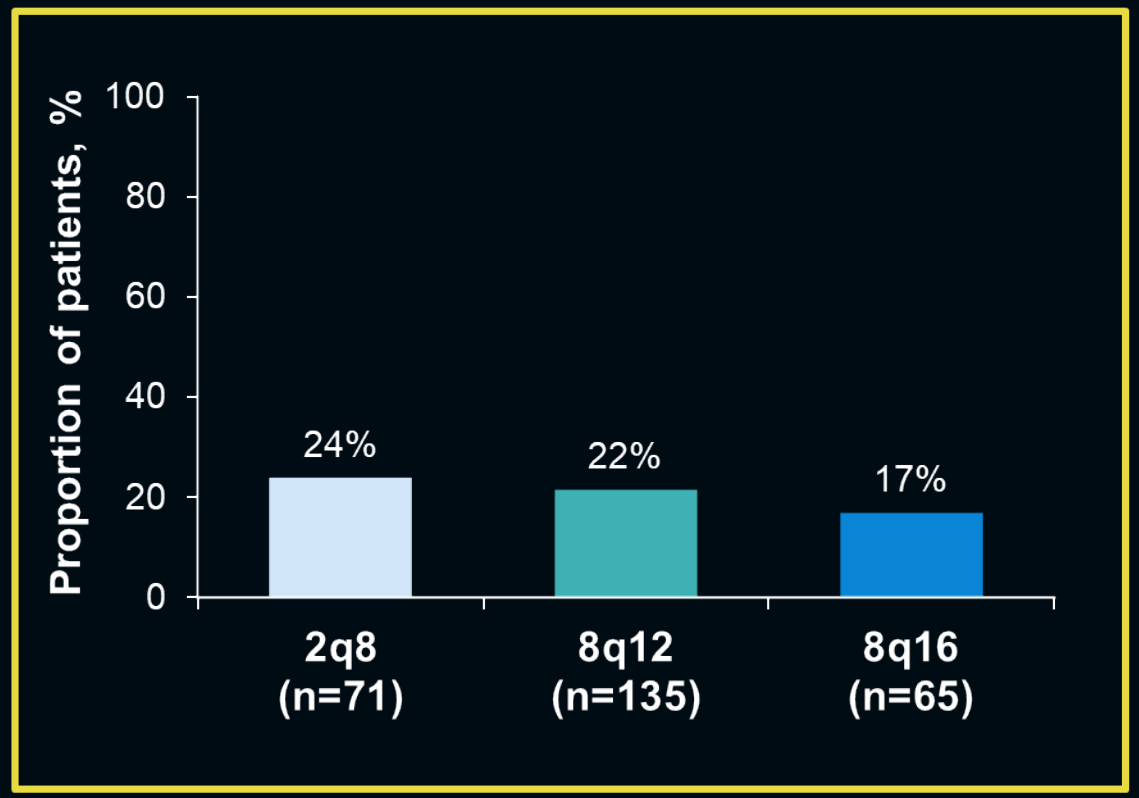
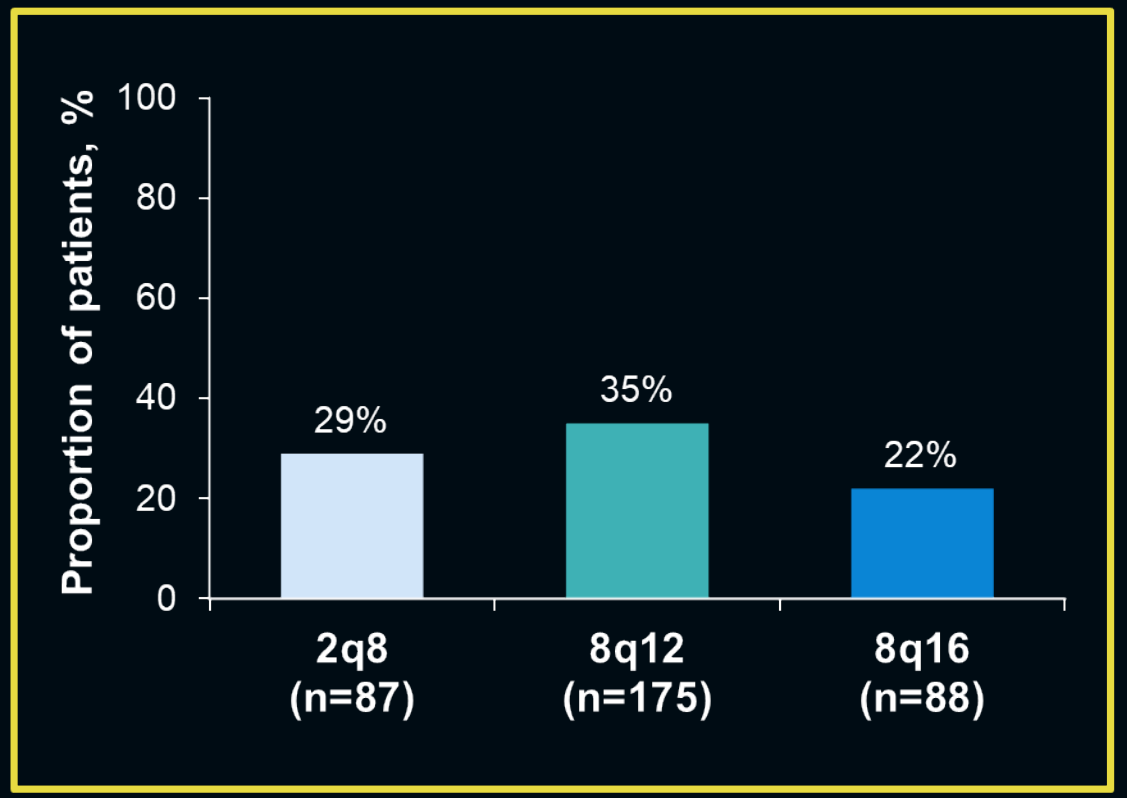
DME

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 48

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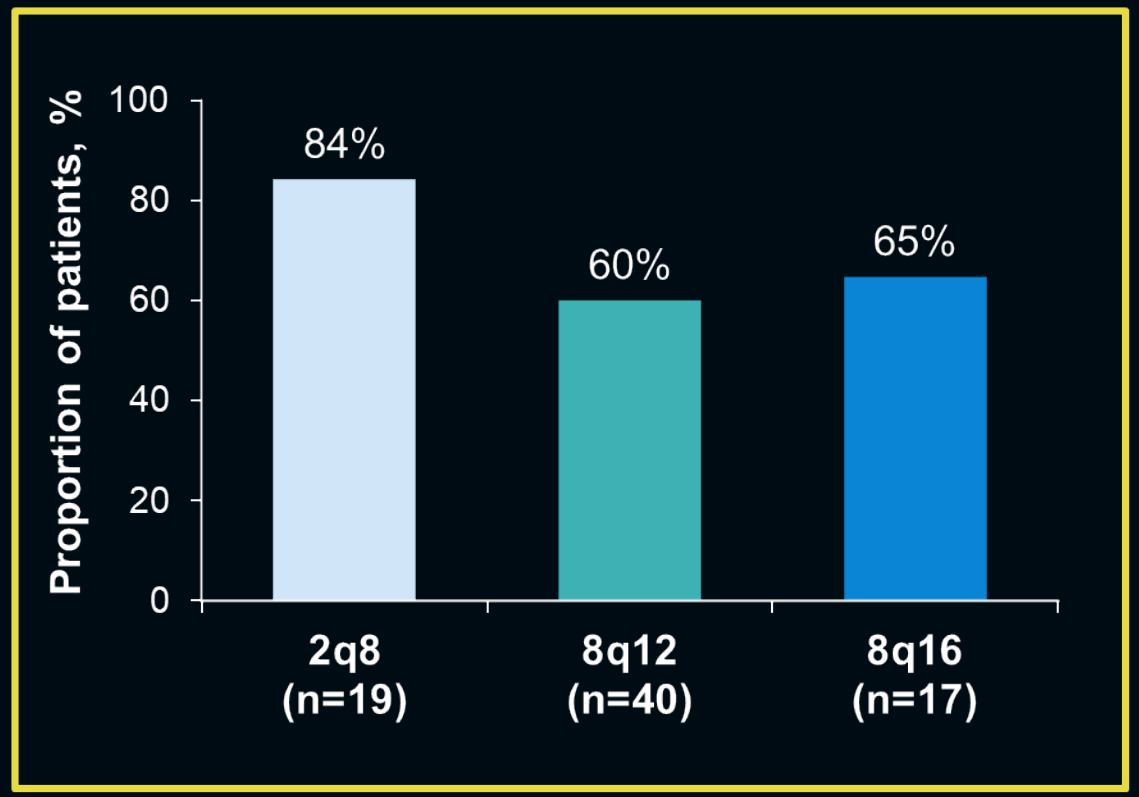
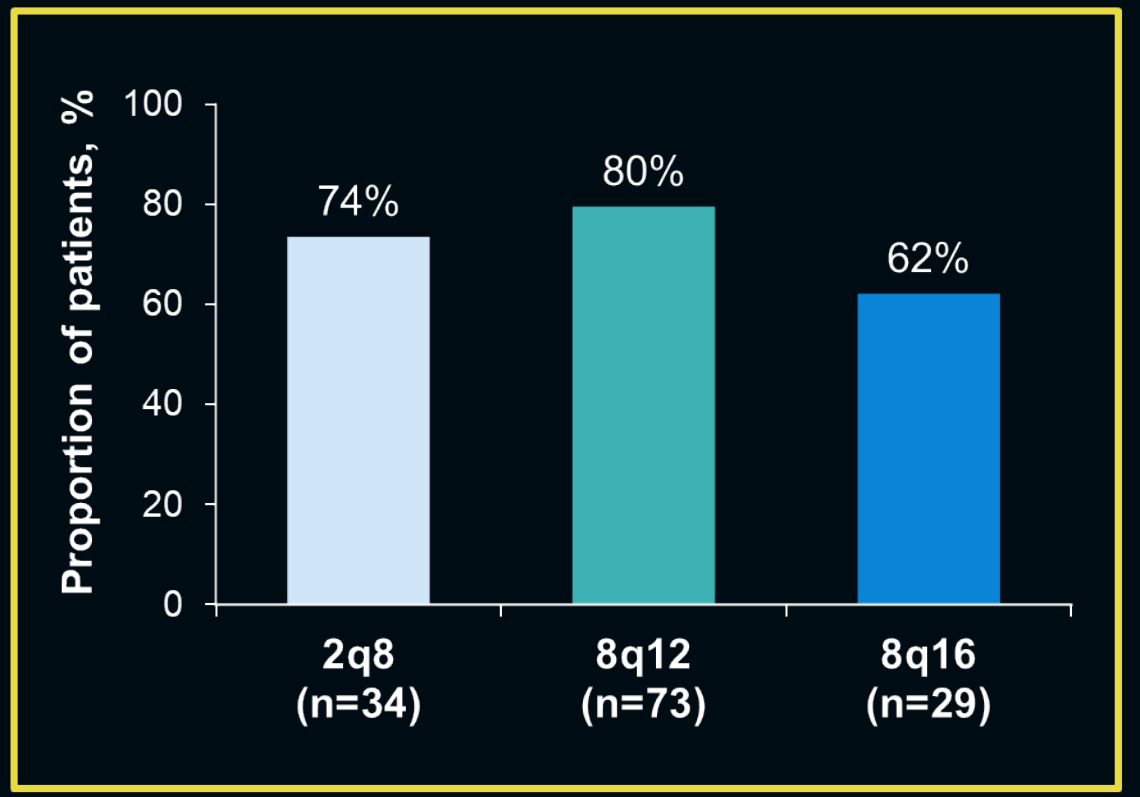
DME

With Prior DME Treatment



Without Prior DME Treatment

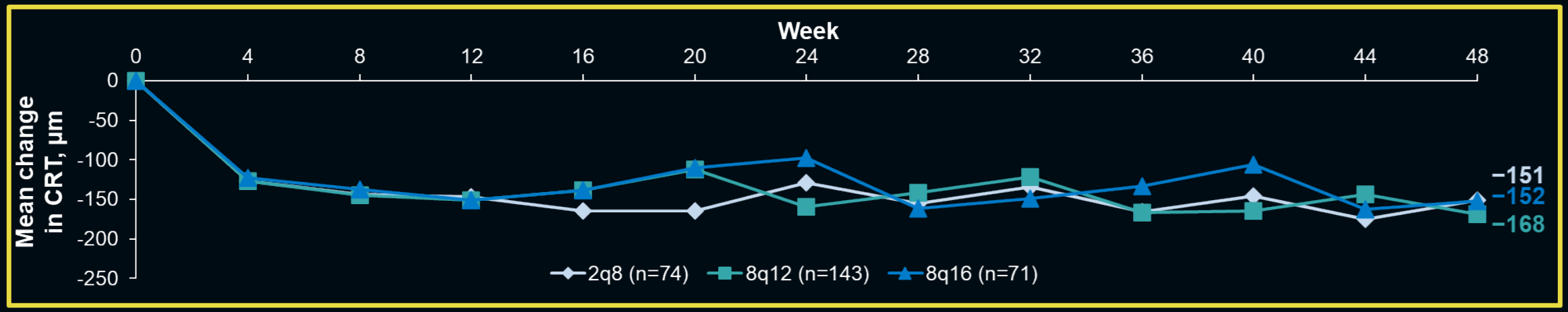


FAS, LOCF.

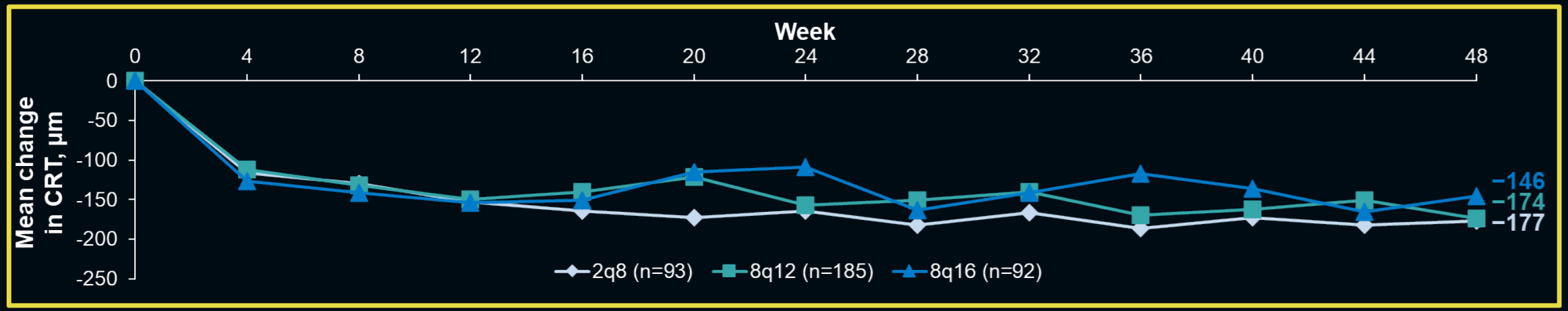
Mean Change in CRT Through Week 48

DME

With Prior DME Treatment



Without Prior DME Treatment



FAS, observed cases.

Proportion of Patients Who Maintained Their Randomized Intervals Through Week 48

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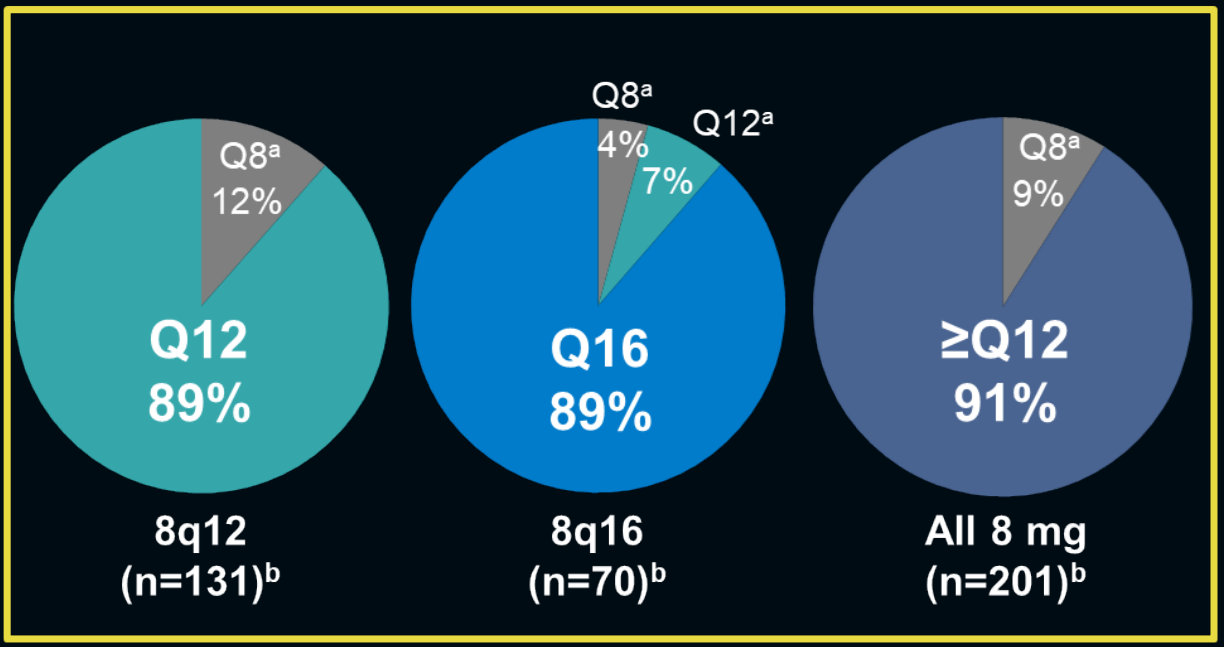
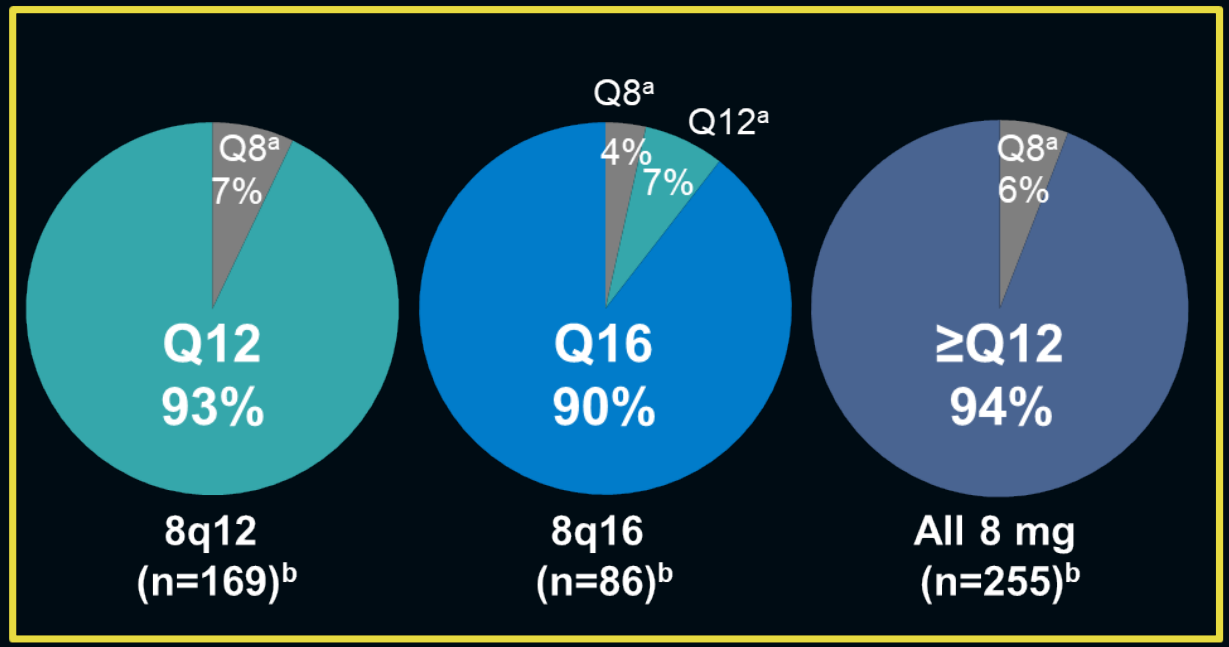
DME

With Prior DME Treatment



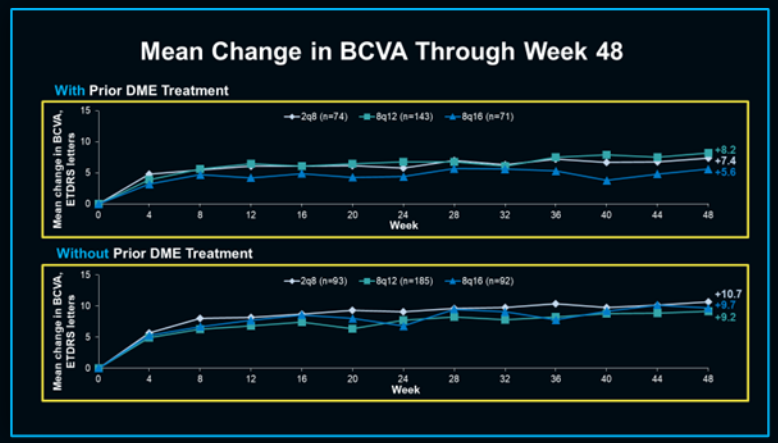
Without Prior DME Treatment

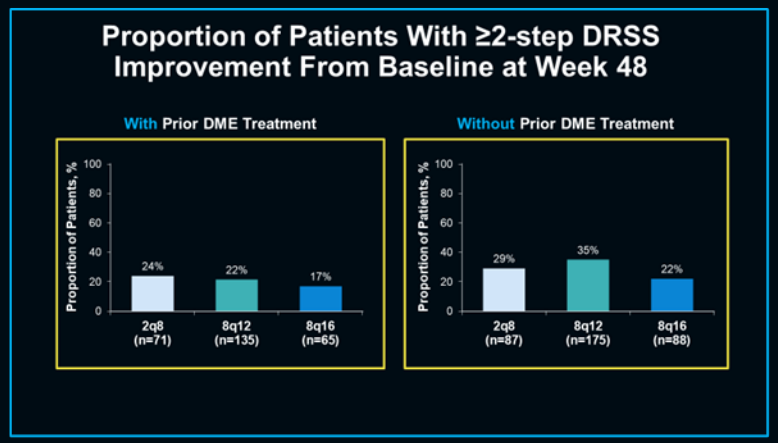


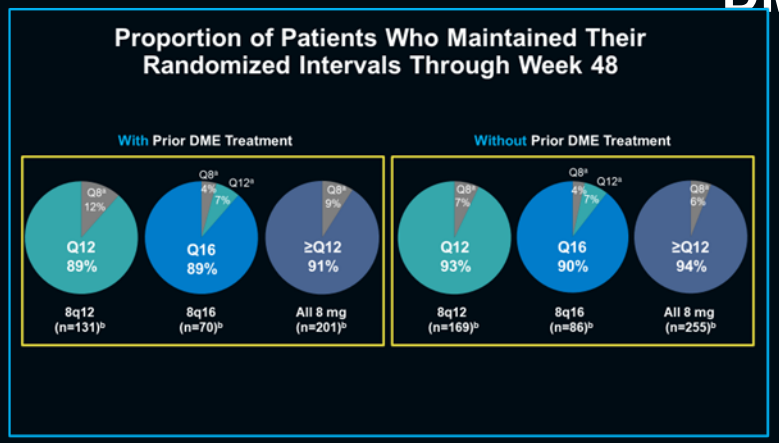
Values may not add up to 100% due to rounding.
[a]Patients whose dosing intervals were shortened based on DRM assessments at some point through Week 48.
[b]Patients completing Week 48.

Conclusions

DME







- BCVA gains and proportions of patients with ≥2-step improvement in DRSS score at Week 48 trended numerically higher across all treatment groups in patients without versus with prior DME treatment
- Outcomes were generally comparable across treatment groups within subgroups of patients with or without prior DME treatment
- Similar proportions of 8q12 and 8q16 patients maintained ≥12-week dosing through Week 48 irrespective of prior DME treatment status