Outcomes of Patients With Diabetic Macular Edema and Baseline Best-Corrected Visual Acuity 20/50 or Worse or 20/40 or Better Treated With Aflibercept 8 mg and 2 mg in the Phase 2/3 PHOTON Trial

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on behalf of the *PHOTON study investigators*

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Disclosures

- Michael Javaheri has acted as a speaker and consultant and has participated in advisory boards with Genentech and Regeneron Pharmaceuticals, Inc.
- Leo A. Kim is on the scientific advisory board for Pykus Therapeutics and INGENIA Therapeutics. Dr Kim has a sponsored research agreement with CureVac AG and Valo Health. Dr Kim receives federal research support from the National Eye Institute and the Department of Defense
- Carol M. Lee has no financial disclosures
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Background

- In the PHOTON trial, aflibercept 8 mg demonstrated non-inferior BCVA gains at Week 48 compared with aflibercept 2 mg, with fewer injections in patients with DME[1]
- However, the impact of baseline BCVA on clinical outcomes following treatment with aflibercept 8 mg is not well characterized

A post hoc analysis was conducted to evaluate visual and anatomic outcomes with aflibercept 8 mg and 2 mg through Week 96 in patients with DME by baseline BCVA (20/50 or worse or 20/40 or better)

BCVA, best-corrected visual acuity; DME, diabetic macular edema.

1. Brown DM et al. *Lancet*. 2024;403:1153-1163.

PHOTON Study Design

Treatment-naive and previously treated patients with center-involved DME[a]

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

	Year 1													Year 2										
	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	Wk 52	Wk 56	Wk 60	Wk 64	Wk 68	Wk 72	Wk 76	Wk 80	Wk 84	Wk 88	Wk 92	Wk 96
2q8	X	X	X	X	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	–
8q12	X	X	X	o	o[a]	X[a]	o	o	X[a]	o	o	X[a]	o	o	X[a,b]	o	o	X[a,b]	o	o	X[a,b]	o	o	X[a,b]	–
8q16	X	X	X	o	o[a]	o[a]	X[a]	o	o	o	X[a]	o	o	o	X[a,b]	o	o	o	X[a, b]	o	o	o	X[a,b]	o	–

Primary endpoint at Wk 48
Mean change in BCVA (non-inferiority)

End of study at Wk 96
With an optional 1-year extension through Wk 156

[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.
2q8, 2 mg every 8 weeks; 8q12, 8 mg every 12 weeks; 8q16, 8 mg every 16 weeks; CRT, central retinal thickness; DRM, dose regimen modification; q8, every 8 weeks; q24, every 24 weeks; Wk, week.

Methods

- This analysis was conducted using data through Week 96 from patients in the FAS, defined as patients who were randomized and treated with aflibercept 8 mg or 2 mg
- Patients were grouped as follows:

Baseline BCVA 20/50 or worse:	<69 ETDRS letters
Baseline BCVA 20/40 or better:	≥69 ETDRS letters

- Key outcomes assessed include:
  - Mean change in BCVA through Week 96
  - Mean change in CRT through Week 96
  - Proportion of patients who maintained or extended their dosing intervals through Week 96
- All analyses were descriptive

ETDRS, Early Treatment Diabetic Retinopathy Study; FAS, full analysis set.

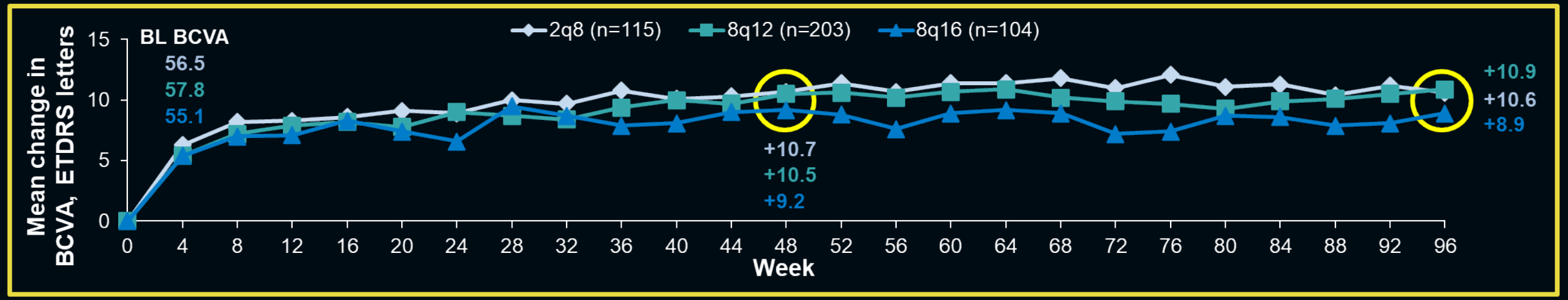
Baseline Characteristics by Baseline BCVA

	Baseline BCVA 20/50 or Worse			Baseline BCVA 20/40 or Better		
	2q8 (n=115)	8q12 (n=203)	8q16 (n=104)	2q8 (n=52)	8q12 (n=125)	8q16 (n=59)
BCVA, mean (SD), ETDRS letters	56.5 (9.9)	57.8 (8.3)	55.1 (10.1)	72.6 (2.9)	73.2 (2.7)	72.6 (2.6)
CRT, mean (SD), µm	482.9 (154.2)	472.7 (136.4)	491.5 (120.4)	400.6 (97.8)	411.1 (100.7)	405.3 (90.8)
Prior DME treatment, n (%)	51 (44.3)	96 (47.3)	53 (51.0)	23 (44.2)	50 (40.0)	18 (30.5)
DRSS score, n (%)						
DRSS 47 or worse	40 (34.8)	73 (36.0)	33 (31.7)	13 (25.0)	40 (32.0)	13 (22.0)
DRSS 43 or better	66 (57.4)	115 (56.7)	62 (59.6)	39 (75.0)	82 (65.6)	45 (76.3)
Non-gradable	9 (7.8)	15 (7.4)	9 (8.7)	0	3 (2.4)	1 (1.7)

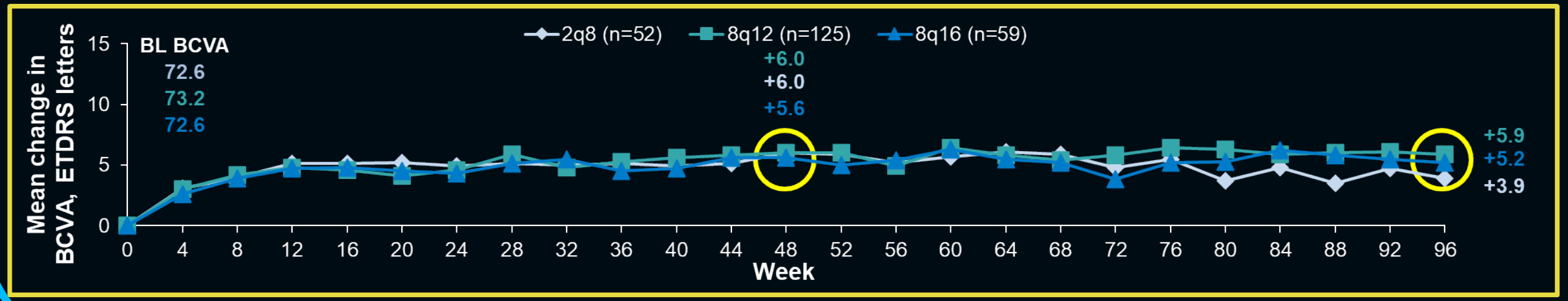
FAS.
DRSS, Diabetic Retinopathy Severity Scale; SD, standard deviation.

Mean Change in BCVA Through Week 96 by Baseline BCVA

Baseline BCVA 20/50 or Worse



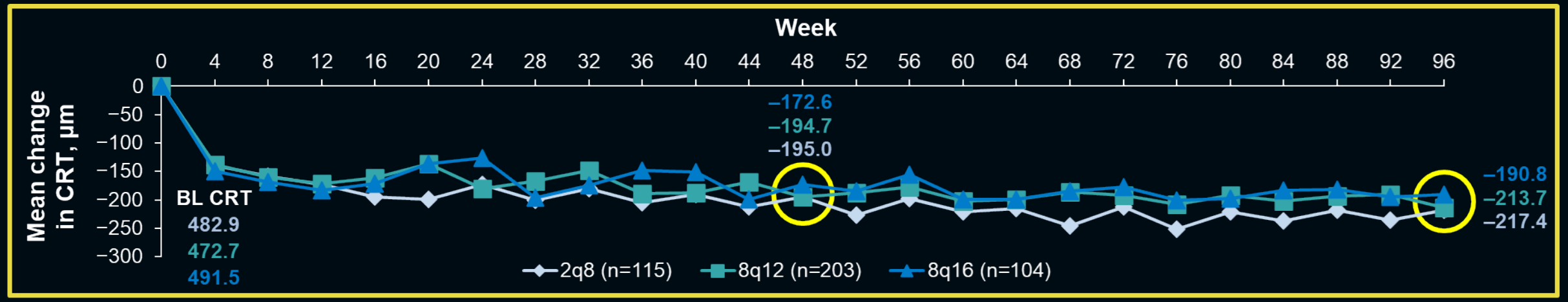
Baseline BCVA 20/40 or Better



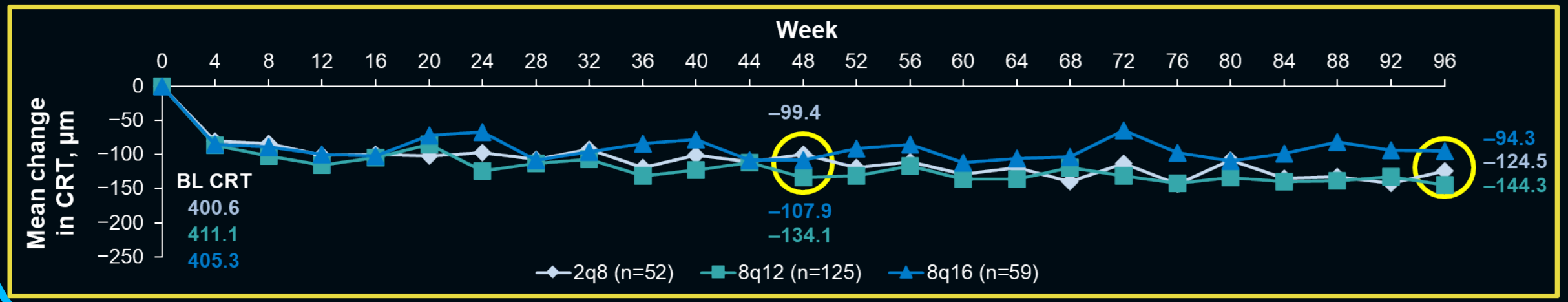
FAS, observed cases.
BL, baseline.

Mean Change in CRT Through Week 96 by Baseline BCVA

Baseline BCVA 20/50 or Worse

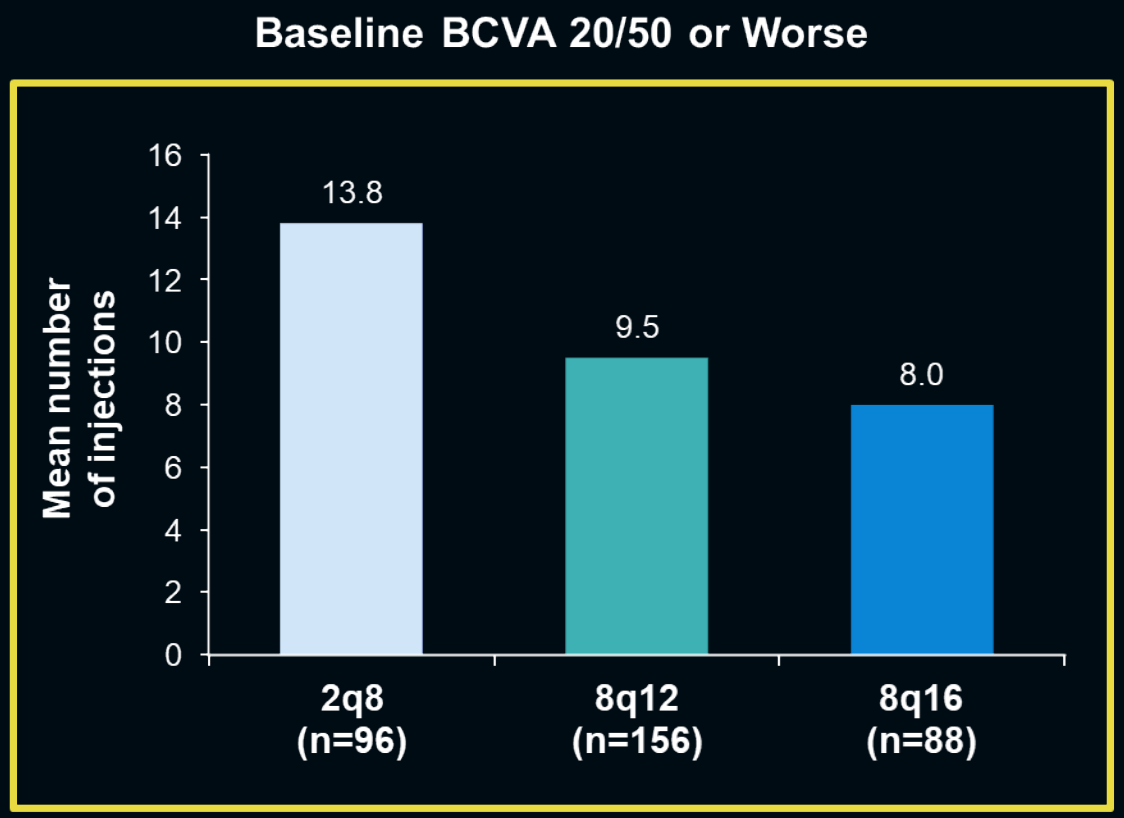


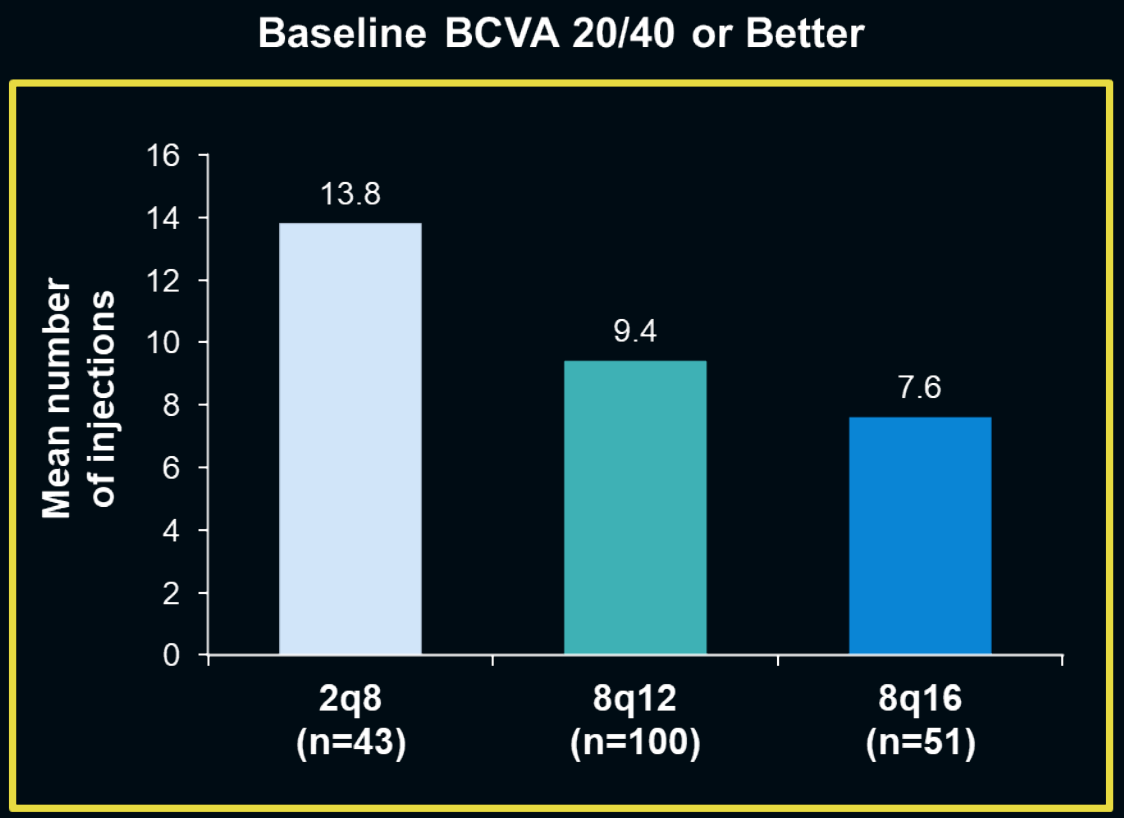
Baseline BCVA 20/40 or Better



FAS, observed cases.

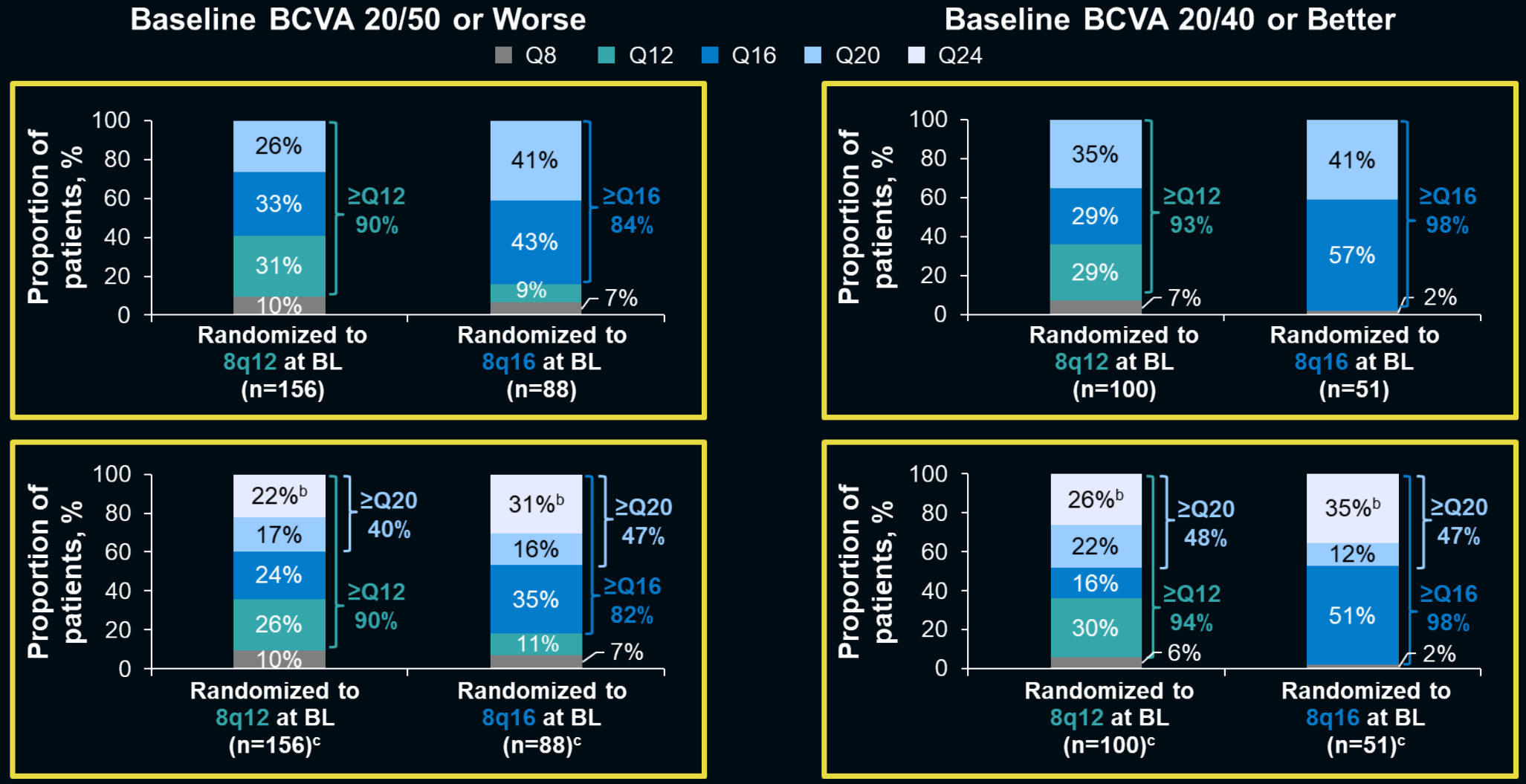
Treatment Exposure Through Week 96 by Baseline BCVA





FAS, patients who completed Week 96.

A Large Proportion of Patients by Baseline BCVA Qualified for an Interval Extension[a] at Week 96



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. [c]Patients completing Week 96.

Q8, every 8 weeks; Q12, every 12 weeks; Q16, every 16 weeks; Q20, every 20 weeks; Q24, every 24 weeks.

Conclusions

- Aflibercept 8 mg demonstrated meaningful visual and anatomic improvements from baseline to Week 96 in patients with DME, with fewer injections, irrespective of baseline BCVA
  - As expected, patients with baseline BCVA 20/50 or worse achieved numerically greater improvements in BCVA and CRT than those with baseline BCVA 20/40 or better with both aflibercept 8 mg and 2 mg
- Most aflibercept 8 mg-treated patients maintained ≥12- and ≥16-week dosing intervals through Week 96, regardless of baseline BCVA
  - At Week 96, approximately 40%-50% of patients had a last assigned dosing interval of ≥20 weeks