Intravitreal Aflibercept 8 mg for Diabetic Macular Edema: Week 96 Efficacy Outcomes by Baseline Characteristics in the Phase 2/3 PHOTON Trial

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Disclosures

- Dr Gill has received consulting fees from Regeneron Pharmaceuticals, Inc. and Roche/Genentech
- The PHOTON study was sponsored by Regeneron Pharmaceuticals, Inc. (Tarrytown, New York) and co-funded by Bayer AG (Leverkusen, Germany). This analysis was funded by Regeneron Pharmaceuticals, Inc. (Tarrytown, NY). The sponsor participated in the design and conduct of the analysis, interpretation of the data, and preparation of this presentation
- 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

- 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]
- The influence of baseline patient demographics and ocular characteristics on the treatment effects of aflibercept 8 mg in patients with DME at 96 weeks in the PHOTON trial have yet to be evaluated

This analysis assessed whether visual improvements achieved with aflibercept 8 mg versus 2 mg at Week 96 in patients with DME in PHOTON were comparable across several patient subgroups

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

1. Brown DM. *Lancet.* 2024:403:1153–1163.

PHOTON Study Design

Multi-center, 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
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)

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

[a]Treatment-naive and previously treated patients with DME.
2q8, 2 mg every 8 weeks; 8q12, 8 mg every 12 weeks; 8q16, 8 mg every 16 weeks.

Patient Baseline Characteristics

	2q8	8q12	8q16	Total
N (FAS/SAF)	167	328	163	658
Age (years)	63.0 (9.8)	62.1 (11.1)	61.9 (9.5)	62.3 (10.4)
Female, %	44.9	36.0	39.3	39.1
Race, %				
White	67.1	70.4	78.5	71.6
Black or African American	10.8	10.7	5.5	9.4
Asian	18.0	14.6	14.1	15.3
Other	2.4	3.0	0.6	2.4
Not reported	1.8	1.2	1.2	1.4
Hispanic or Latino, %	18.6	16.5	20.9	18.1
Duration of diabetes (years)	15.9 (10.0)	15.1 (10.0)	15.7 (10.7)	15.5 (10.2)
Hemoglobin A1c (%)	8.1 (1.5)	7.9 (1.5)	7.8 (1.5)	8.0 (1.5)
History of hypertension, %	77.8	77.4	79.8	78.1
BMI (kg/m^2)	29.9 (6.5)	30.4 (6.2)	31.0 (6.1)	30.5 (6.2)

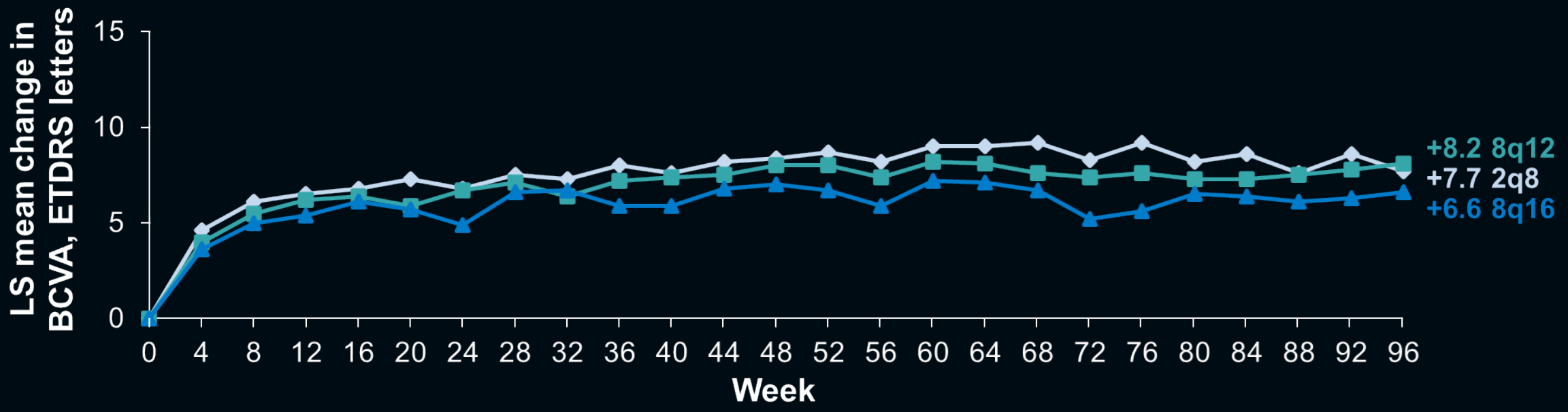
Data are mean (SD) unless otherwise indicated.
BMI, body mass index; FAS, full analysis set; SAF, safety analysis set; SD, standard deviation.

Baseline Characteristics of the Study Eye

	2q8	8q12	8q16	Total
N (FAS/SAF)	167	328	163	658
BCVA (ETDRS letters)	61.5 (11.2)	63.6 (10.1)	61.4 (11.8)	62.5 (10.9)
Snellen equivalent	20/63	20/50	20/63	20/63
20/32 (>73 to 78 ETDRS letters), %	12.0	18.0	14.1	15.5
20/40 or worse (≤73 ETDRS letters), %	88.0	82.0	85.9	84.5
CRT (μm)	457.2 (144.0)	449.1 (127.4)	460.3 (117.8)	454.0 (129.5)
Prior treatment for DME, %	44.3	44.5	43.6	44.2

Data are mean (SD) unless otherwise indicated.
CRT, central retinal thickness; ETDRS, Early Treatment of Diabetic Retinopathy Study.

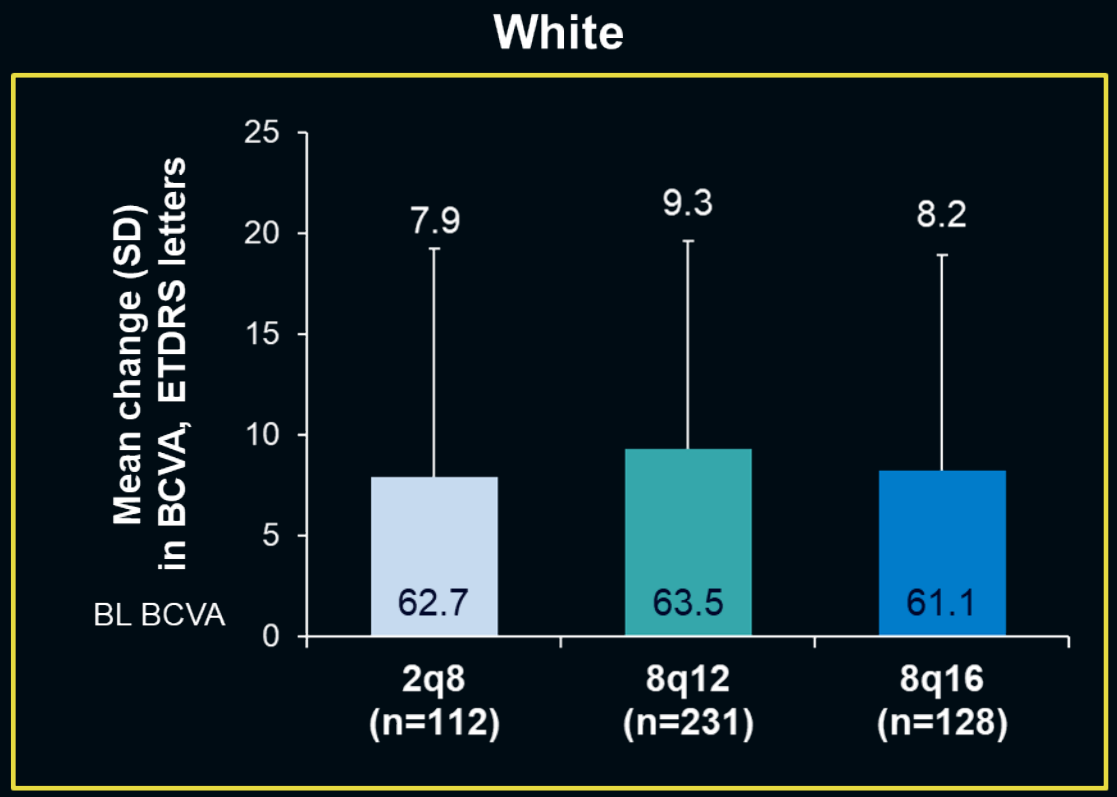
Mean Change in BCVA at Week 96

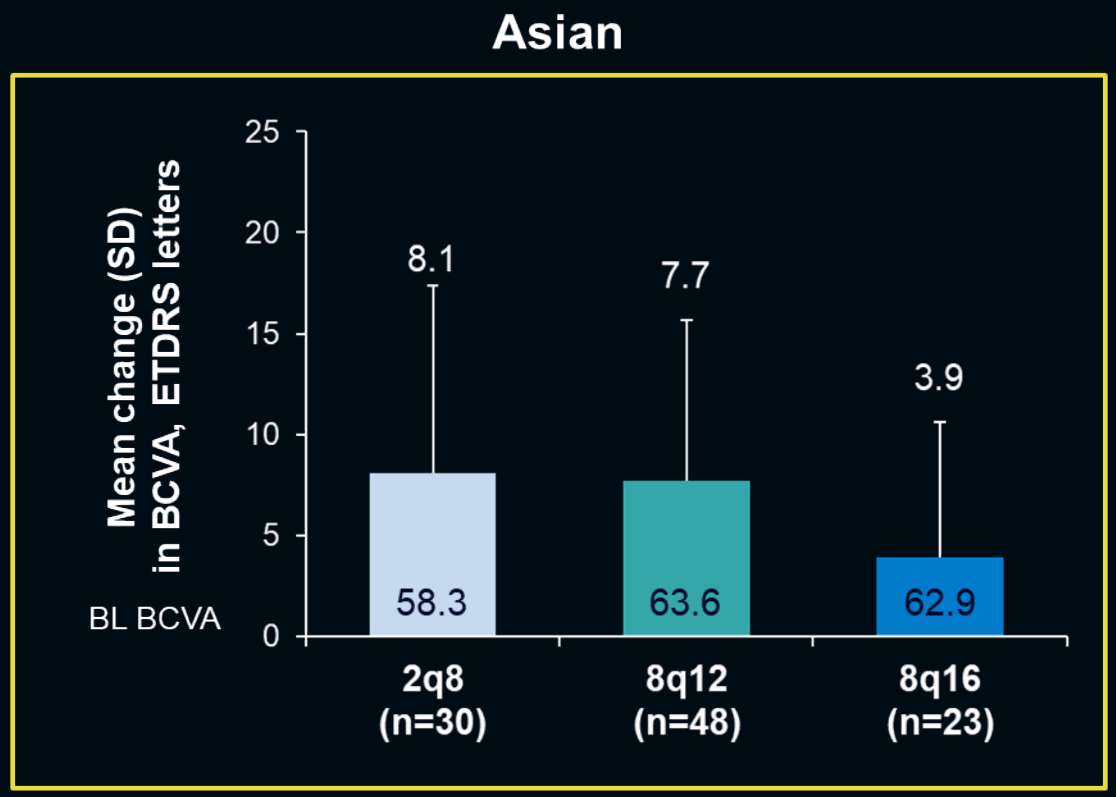


	Mean number of injections[a]	LS mean change from BL at **Week 96** (MMRM)	Diff. in LS means vs 2q8	2-sided 95% CI	1-sided test for non-inferiority at 4-letter margin
2q8	13.8	7.7			
8q12	9.5	8.2	**+0.45**	**–1.55, 2.45**	***P*<0.0001 (nominal)**
8q16	7.8	6.6	**–1.11**	**–3.27, 1.05**	***P*=0.0044 (nominal)**

Data shown in the figure represent LS mean values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at BL).
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 CRT [<400 µm vs ≥400 µm], prior treatment for DME [yes vs no]) as fixed factors, and interaction terms for BL and visit and for treatment and visit.
[a]Patients completing Week 96: 2q8 n=139; 8q12 n=256; 8q16 n=139.
BL, baseline; CI, confidence interval; Diff., difference; ICE, intercurrent event; LS, least squares; MMRM, mixed model for repeated measures.

Mean Change in BCVA at Week 96 by Race[a]

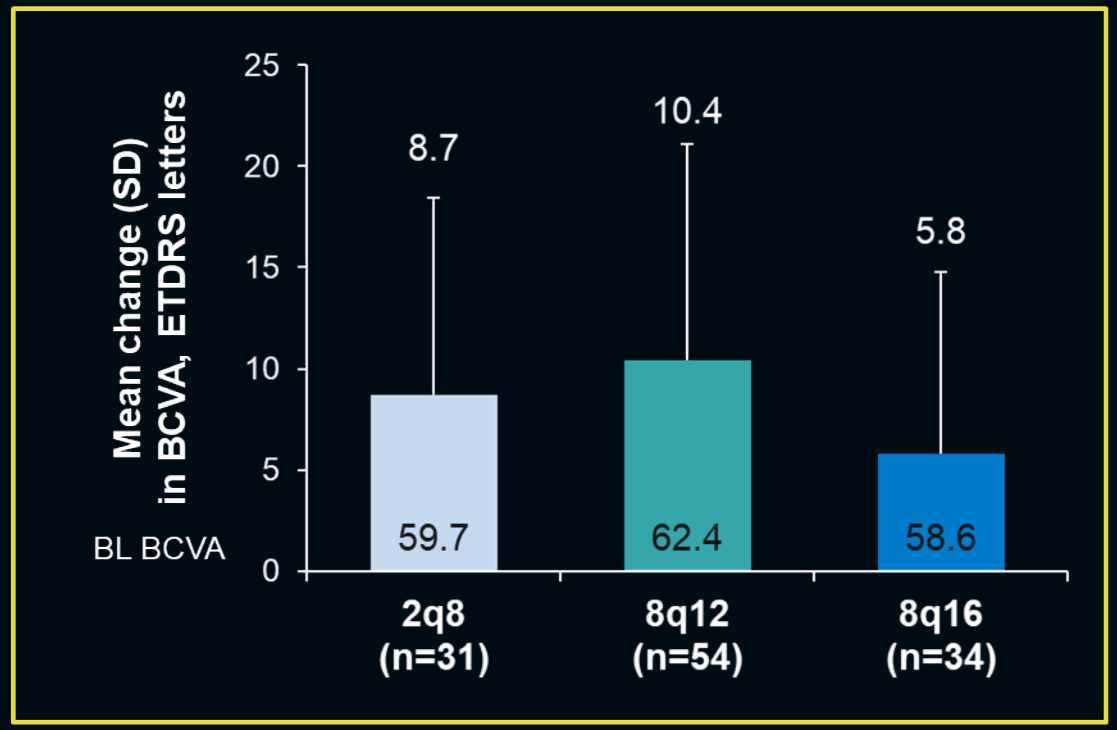




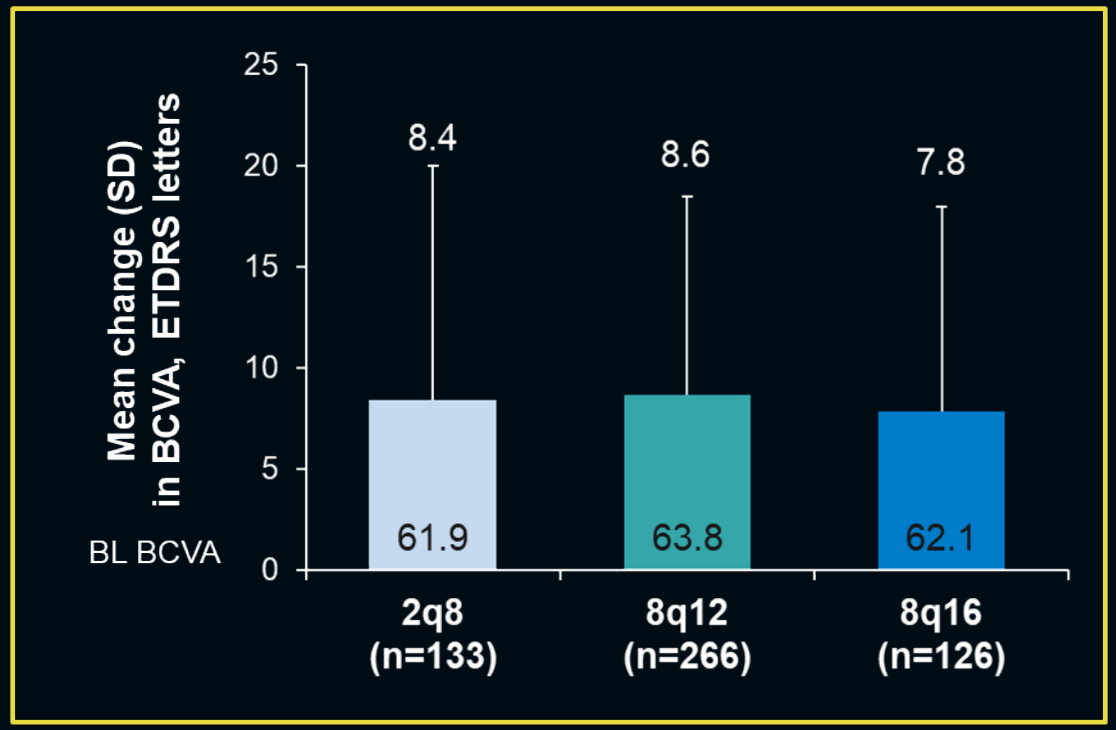
FAS, observed cases (censoring data post-ICE). At BL, 2q8: n=167; 8q12: n=328; 8q16: n=163.
[a]The Black or African American race subgroup could not be evaluated due to the small sample size (<20 patients in the 2q8 and 8q16 groups).

Mean Change in BCVA at Week 96 by Ethnicity

Hispanic or Latino

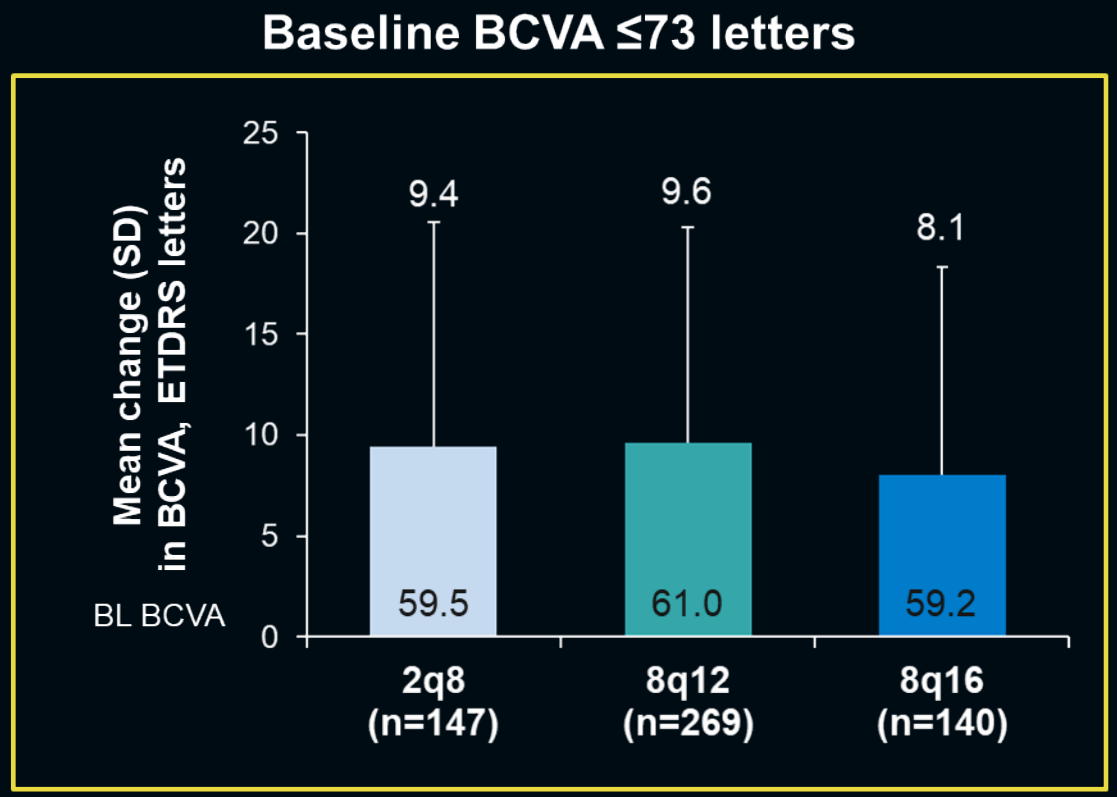


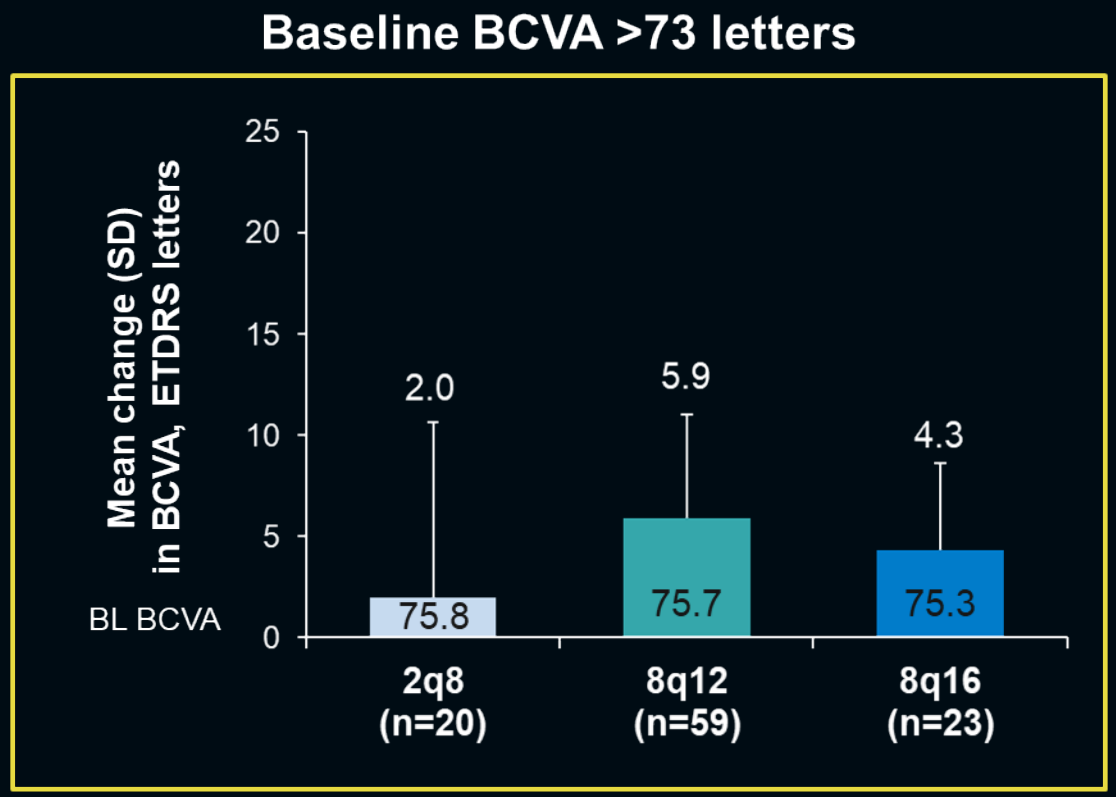
Not Hispanic or Latino



FAS, observed cases (censoring data post-ICE). At BL, 2q8: n=167; 8q12: n=328; 8q16: n=163.

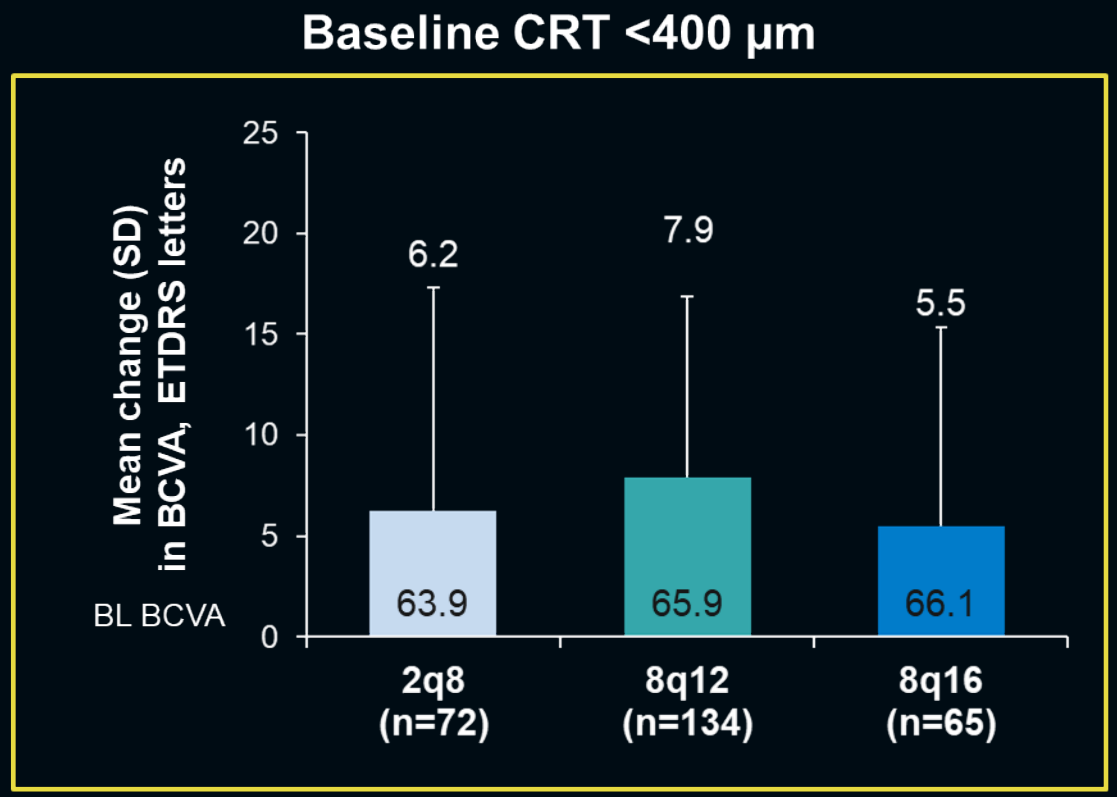
Mean Change in BCVA at Week 96 by Baseline BCVA

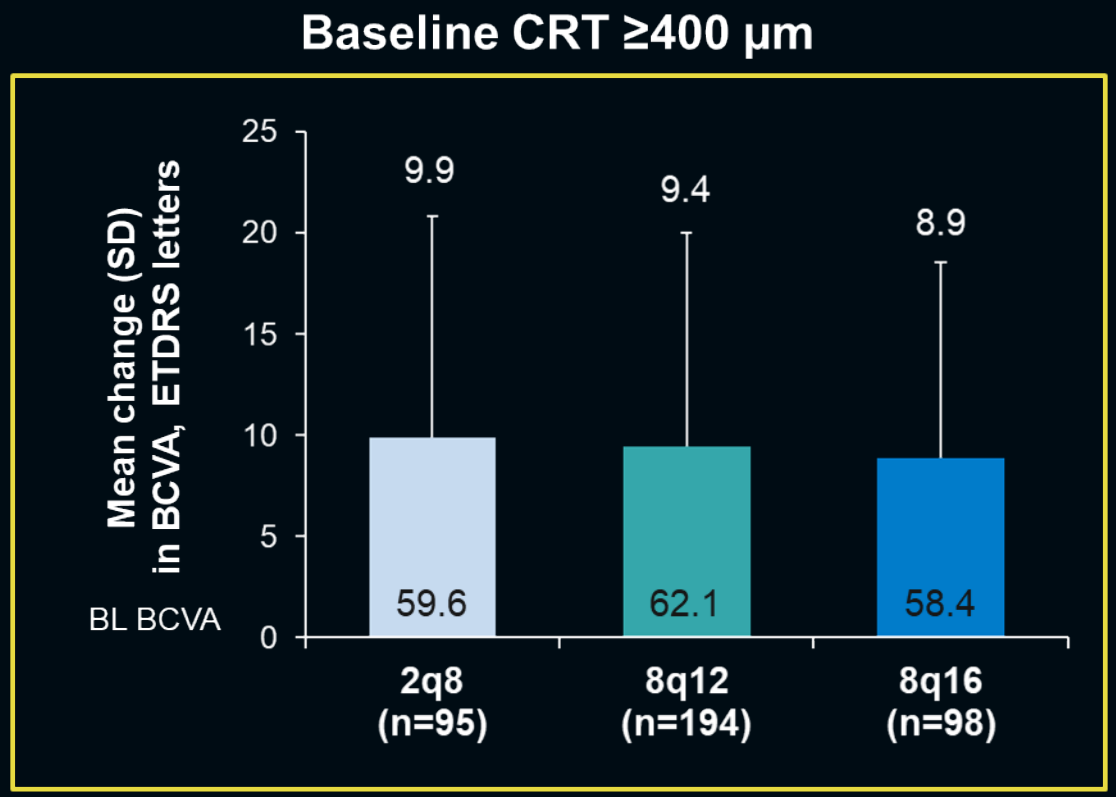




FAS, observed cases (censoring data post-ICE). At BL, 2q8: n=167; 8q12: n=328; 8q16: n=163.

Mean Change in BCVA at Week 96 by Baseline CRT

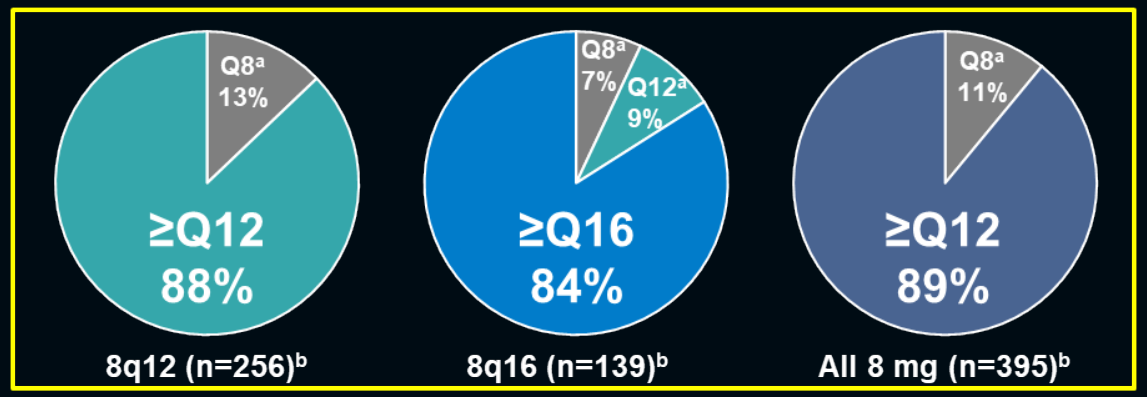




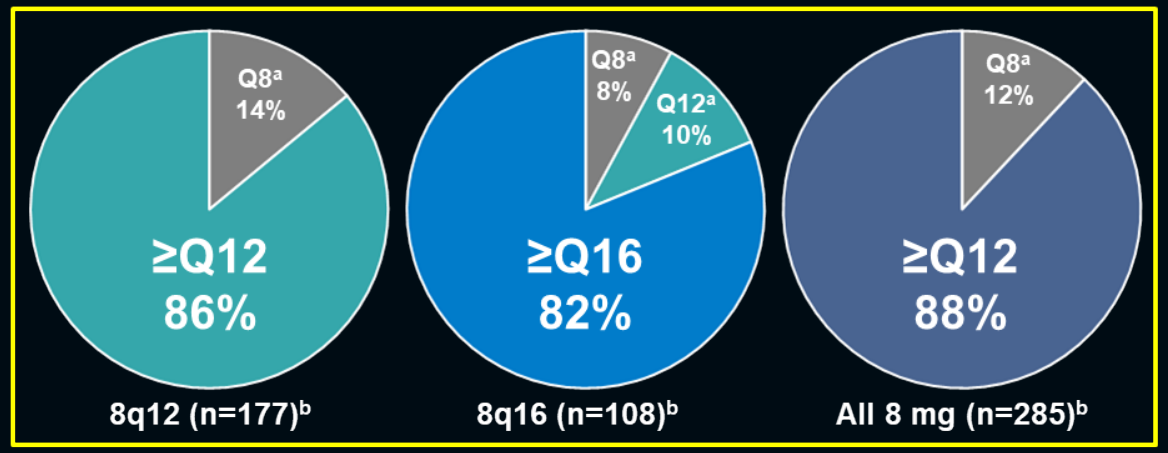
FAS, observed cases (censoring data post-ICE). At BL, 2q8: n=167; 8q12: n=328; 8q16: n=163.

Proportion of 8 mg Patients Who Maintained Randomized Dosing Intervals Through Week 96 by Race

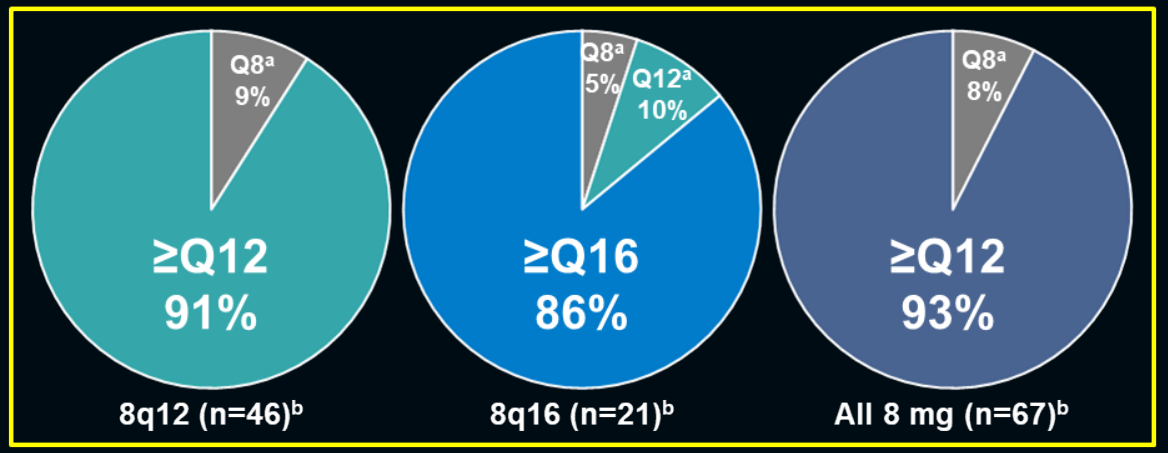
All Patients



White Patients



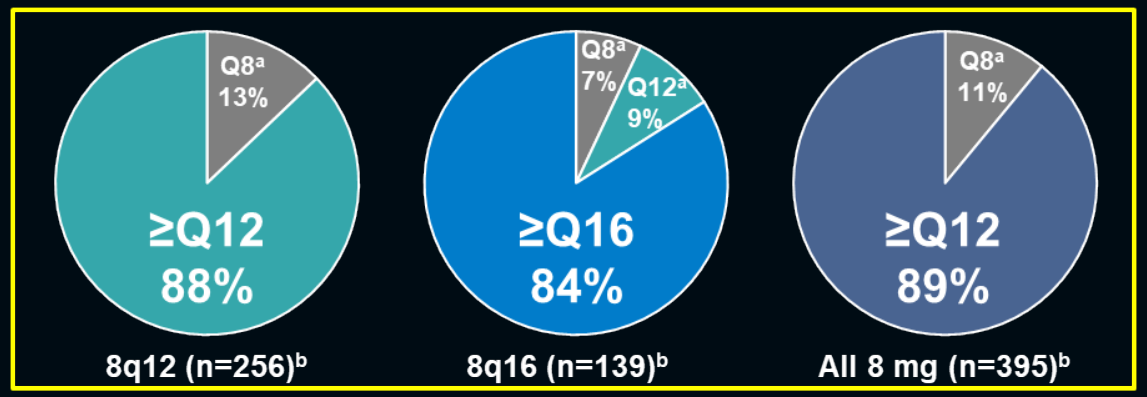
Asian Patients



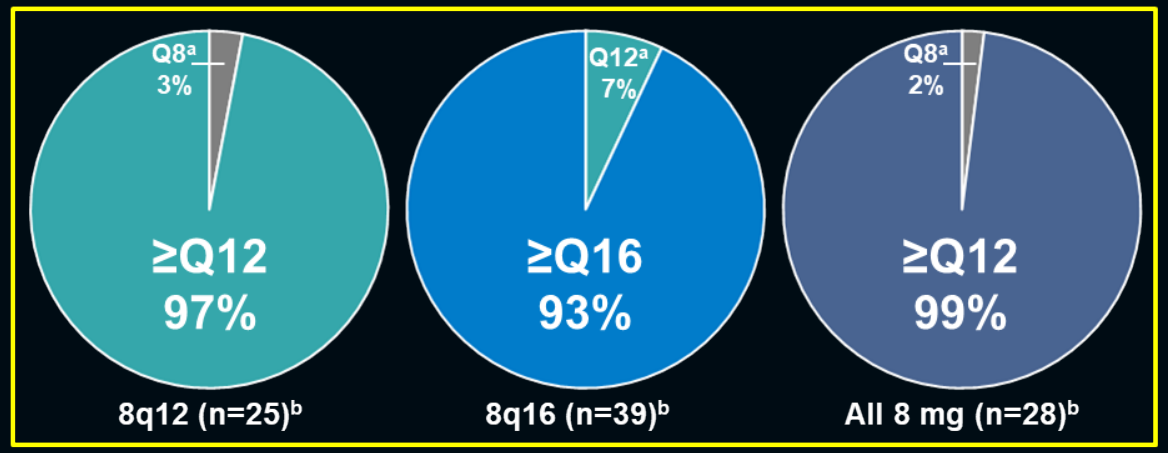
Values may not add up to 100% due to rounding. Data are not reported for Black or African American patients due to the small sample size.
[a]Patients shortened based on DRM criteria through Week 96. [b]Patients completing Week 96.

Proportion of 8 mg Patients Who Maintained Randomized Dosing Intervals Through Week 96 by Ethnicity

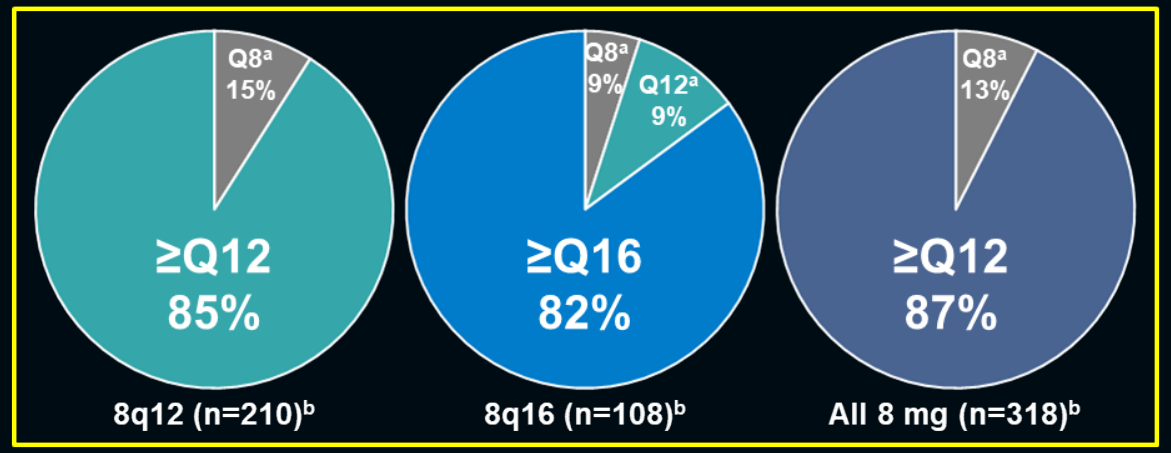
All Patients



Hispanic or Latino Patients



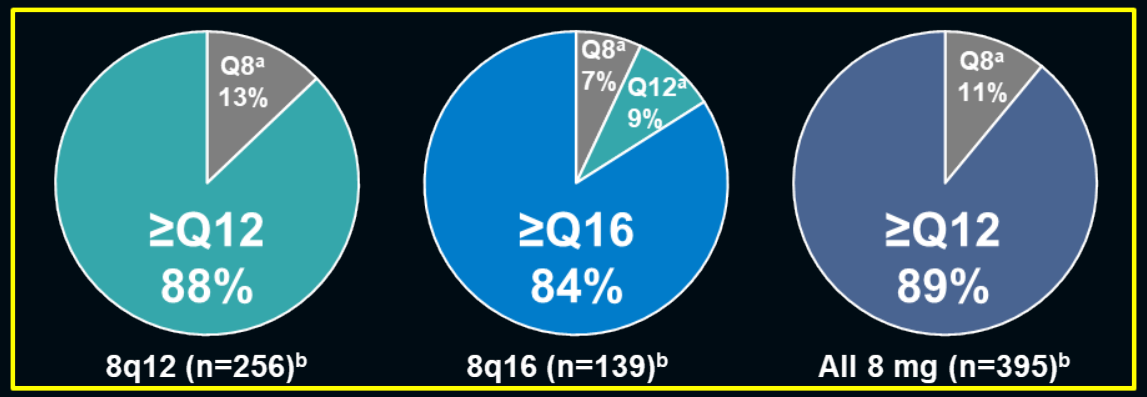
Not Hispanic or Latino Patients



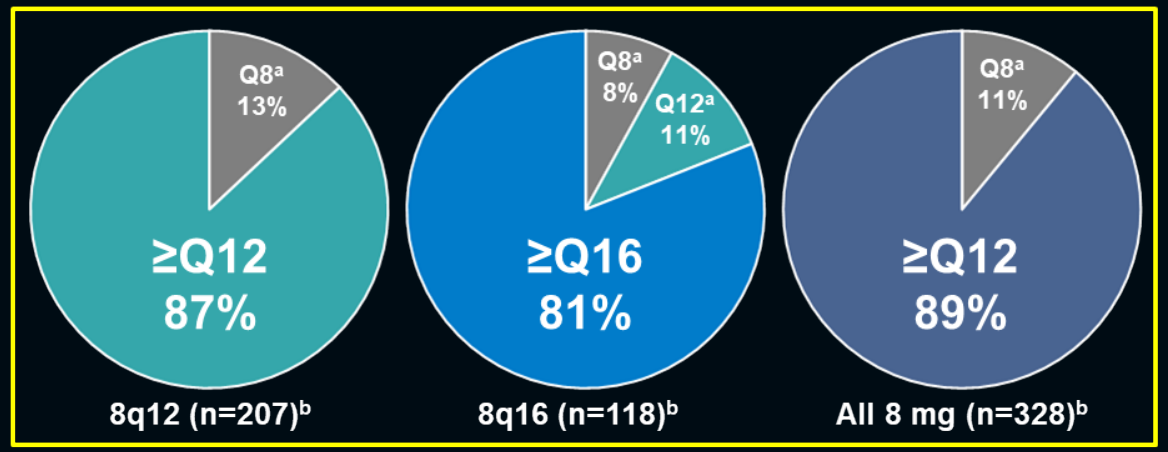
Values may not add up to 100% due to rounding.
[a]Patients shortened based on DRM criteria through Week 96. [b]Patients completing Week 96.

Proportion of 8 mg Patients Who Maintained Randomized Dosing Intervals Through Week 96 by BL BCVA

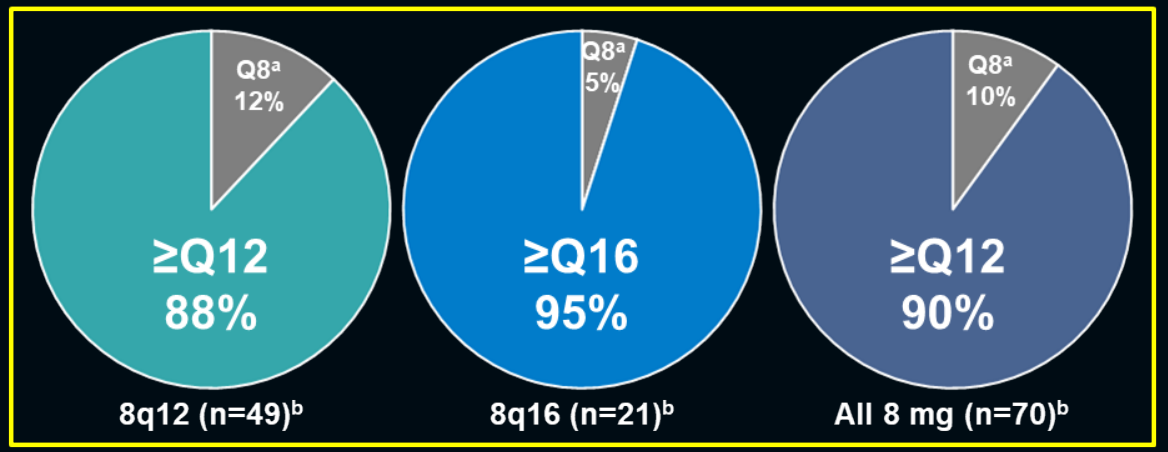
All Patients



BL BCVA ≤73 Letters



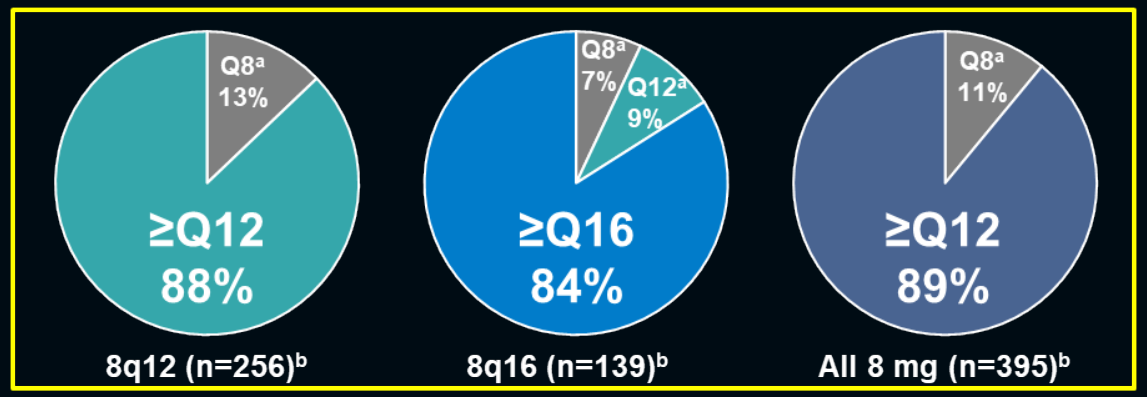
BL BCVA >73 Letters



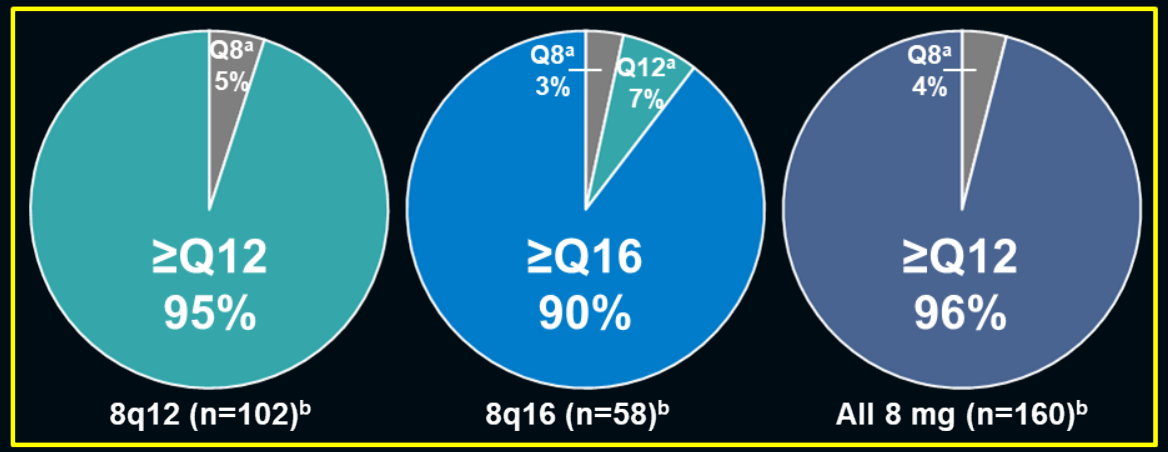
Values may not add up to 100% due to rounding.
[a]Patients shortened based on DRM criteria through Week 96. [b]Patients completing Week 96.

Proportion of 8 mg Patients Who Maintained Randomized Dosing Intervals Through Week 96 by BL CRT

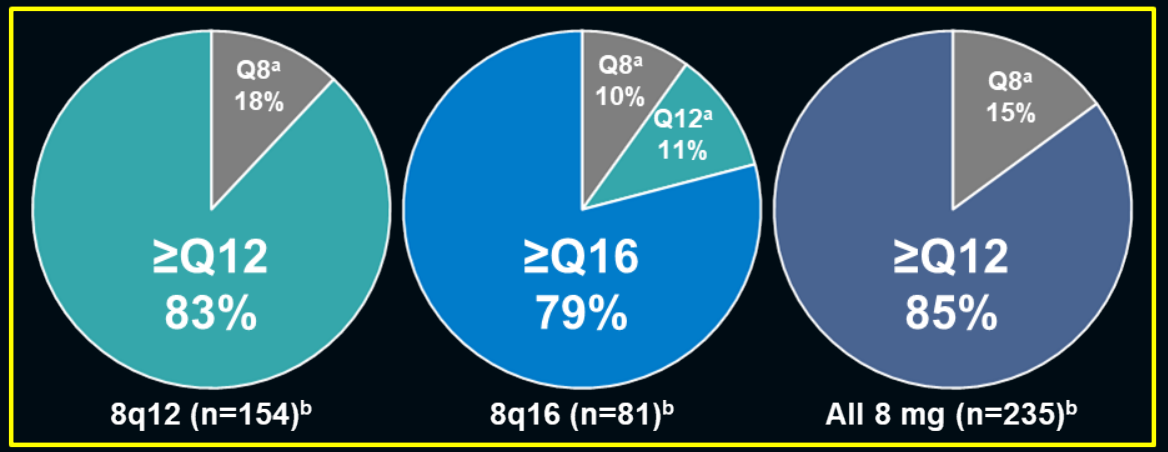
All Patients



BL CRT <400 µm



BL CRT ≥400 µm



Values may not add up to 100% due to rounding.
[a]Patients shortened based on DRM criteria through Week 96. [b]Patients completing Week 96.

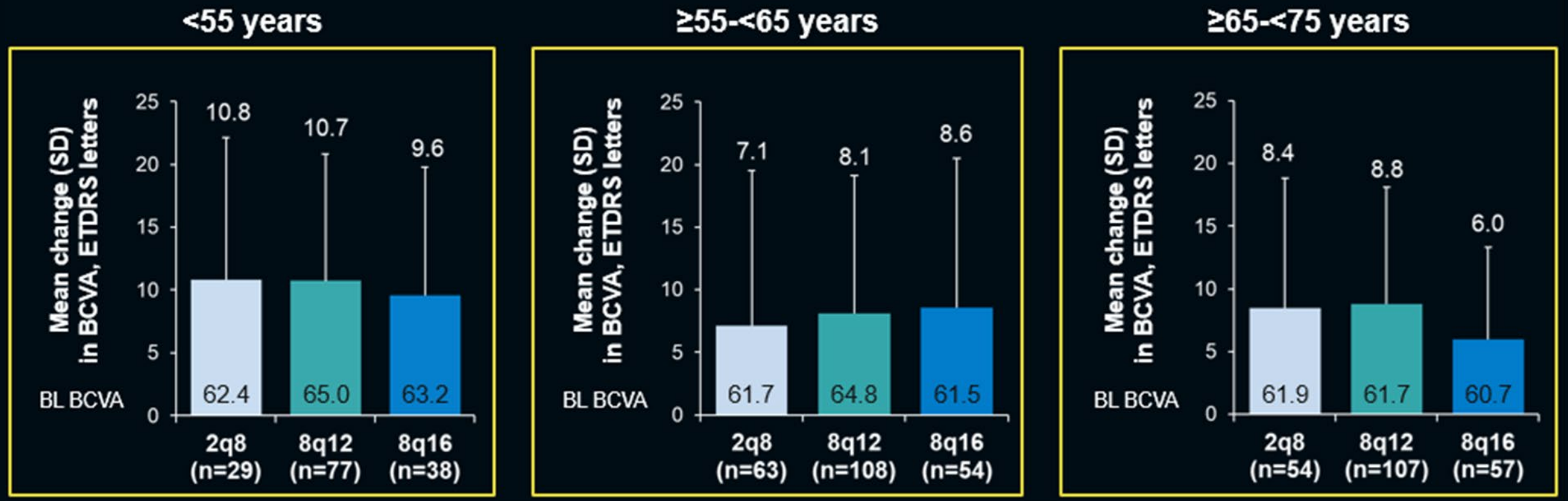
Limitations

- This analysis was not designed to evaluate statistical differences within subgroups
- Select subgroups (age ≥75 years and Black or African American race) could not be evaluated due to the small sample size

Conclusions

- Aflibercept 8 mg achieved meaningful BCVA gains from baseline at Week 96 in patients with DME across evaluable subgroups of race, ethnicity, baseline BCVA, and baseline CRT
- Similar proportions of patients across subgroups were able to achieve dosing intervals of 12 weeks or longer

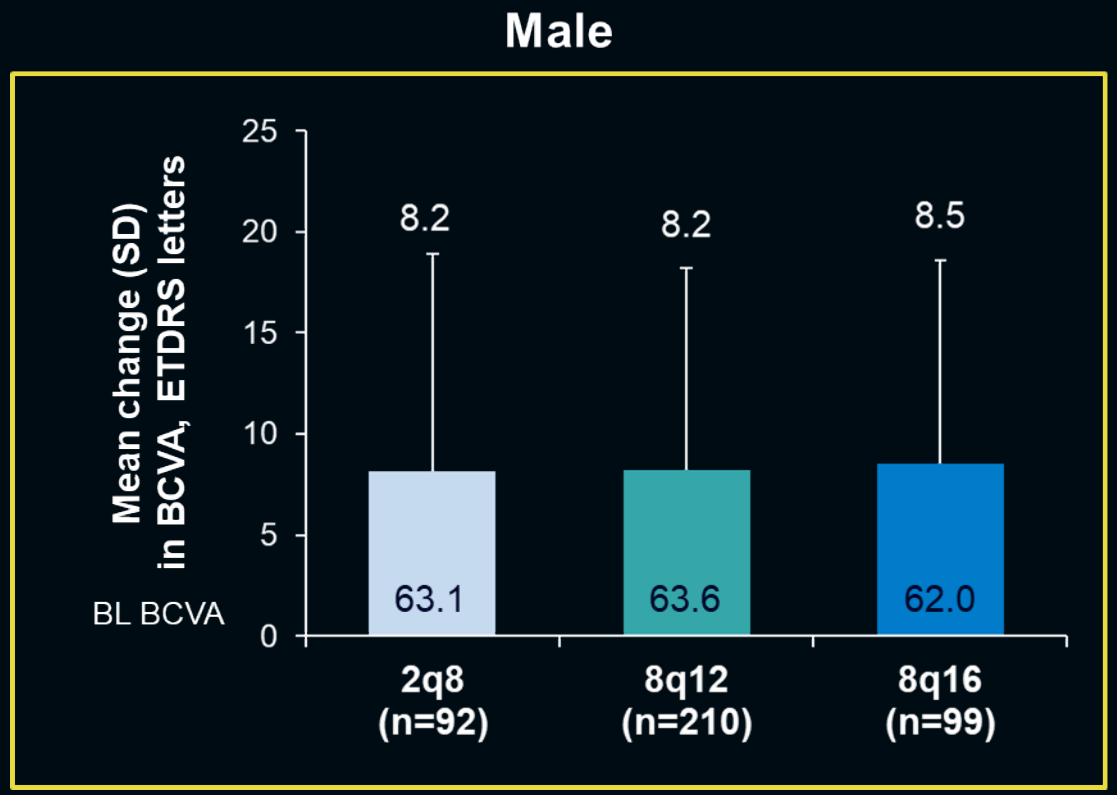
Mean Change in BCVA at Week 96 by Age[a]

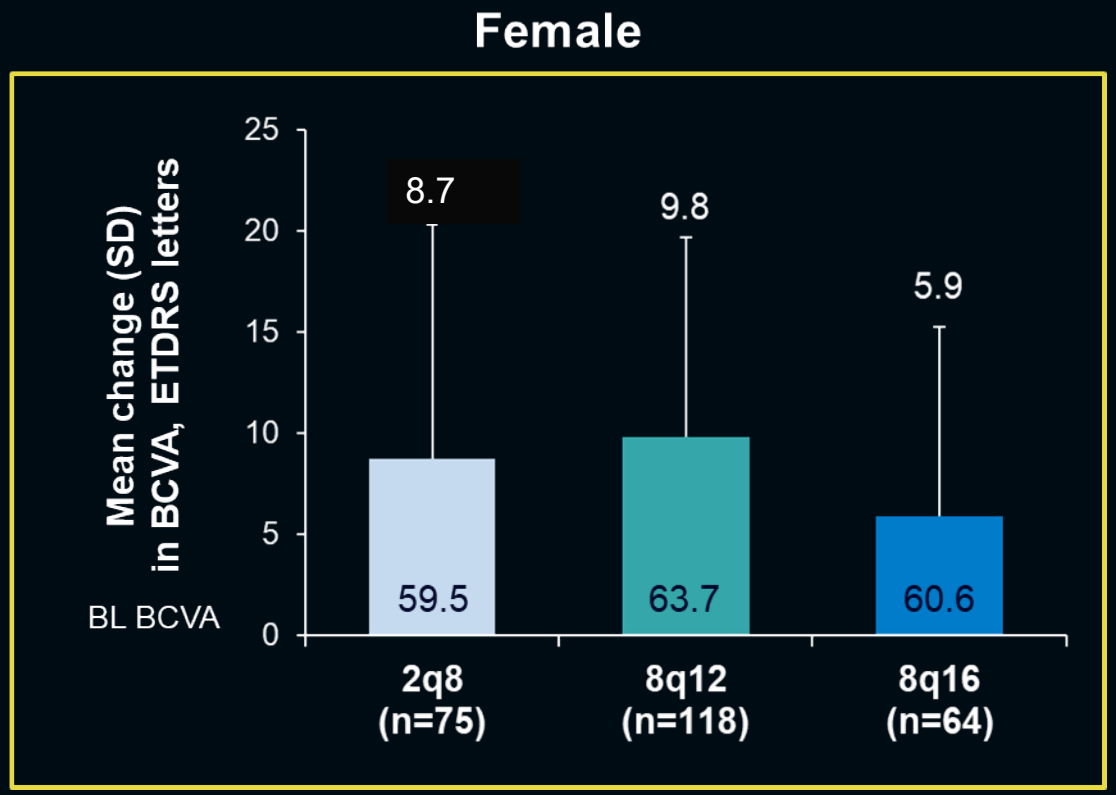


FAS, observed cases (censoring data post-ICE). At BL, 2q8: n=167; 8q12: n=328; 8q16: n=163.

[a]The age ≥75 years subgroup could not be evaluated due to the small sample size (<20 patients in the 2q8 and 8q16 treatment groups).

Mean Change in BCVA at Week 96 by Sex





FAS, observed cases (censoring data post-ICE). At BL, 2q8: n=167; 8q12: n=328; 8q16: n=163.