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

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- Data originally presented at the Retina World Congress; May 9-12, Fort Lauderdale, FL, USA

Background and Study Design

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- 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 aflibercept 2 mg at Week 96 in patients with DME in PHOTON were comparable across several patient subgroups

PHOTON

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; BCVA, best-corrected visual acuity; DME, diabetic macular edema.
1. Brown DM. *Lancet.* 2024:403:1153–1163.

Baseline Demographics and Ocular Characteristics of the Study Eye

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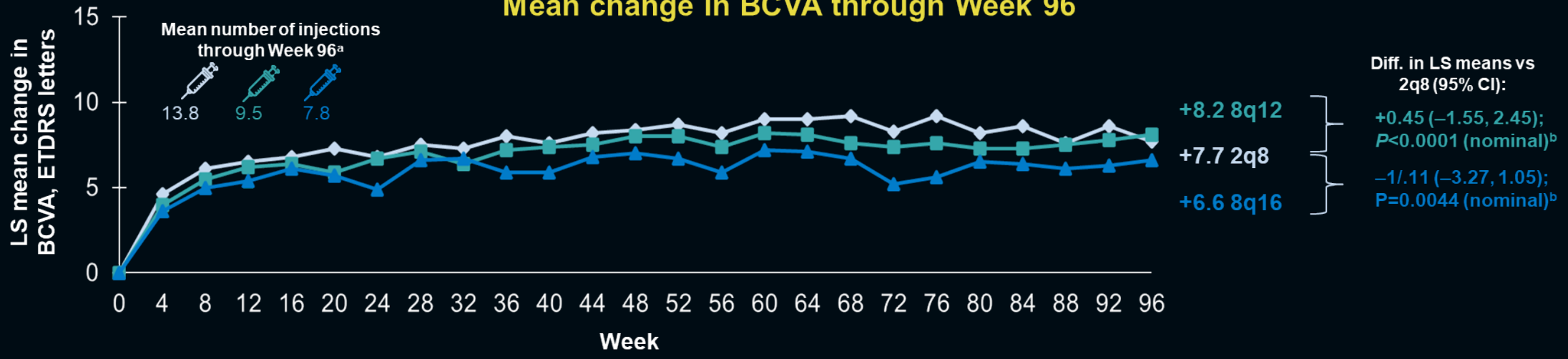
	2q8	8q12	8q16	Total
N (FAS/SAF)	**167**	**328**	**163**	**658**
Age (years)	63.0 (9.8)	62.1 (11.1)	61.9 (9.5)	62.3 (10.4)
Female (%)	44.9%	36.0%	39.3%	39.1%
Race (%)				
White	67.1%	70.4%	78.5%	71.6%
Black or African American	10.8%	10.7%	5.5%	9.4%
Asian	18.0%	14.6%	14.1%	15.3%
Other	2.4%	3.0%	0.6%	2.4%
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)
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%	43.6%	43.6%	43.8%

Data are mean (SD) unless otherwise indicated.
BMI, body mass index; CRT, central retinal thickness; ETDRS, Early Treatment of Diabetic Retinopathy Study; FAS, full analysis set; SAF, safety analysis set; SD, standard deviation.

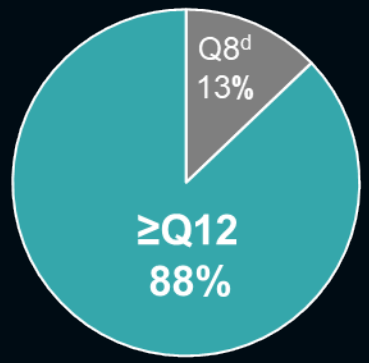
Mean Change in BCVA and Proportion of Patients Maintaining Randomized Treatment Intervals at Week 96

DME

Mean change in BCVA through Week 96

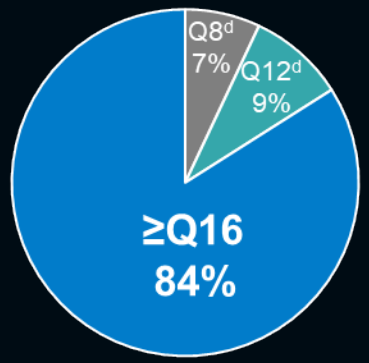


Proportion of patients treated with aflibercept 8 mg who maintained randomized intervals through Week 96[c]



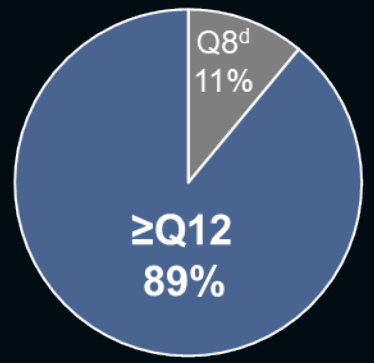
88% of patients in the 8q12 group maintained ≥12-week intervals

Randomized to 8q12 at BL (n=256)[e]



84% of patients in the 8q16 group maintained ≥16-week intervals

Randomized to 8q16 at BL (n=139)[e]



All 8 mg (n=395)[e]

Mean change in BCVA through Week 96: Data shown 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.

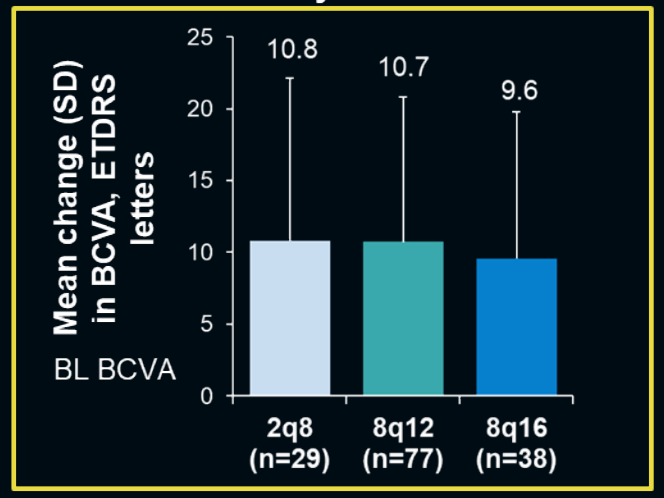
[a]Patients completing Week 96: 2q8 n=139; 8q12 n=256; 8q16 n=139. [b]1-sided test for non-inferiority at 4-letter margin. [c]Values may not add up to 100% due to rounding. [d]Patients met DRM criteria for dosing interval shortening at some point through Week 96. [e]Patients completing Week 96. BL, baseline; CI, confidence interval; DRM, dose regimen modification; ICE, intercurrent event; LS, least squares; MMRM, mixed model for repeated measures.

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

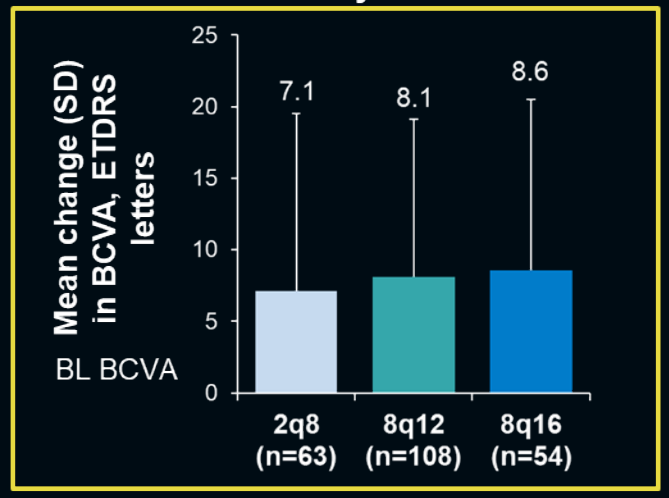
DME

Age

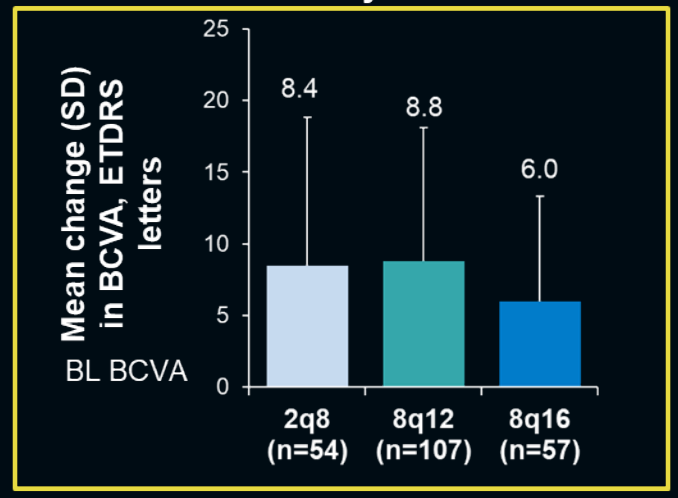
<55 years



≥55-<65 years

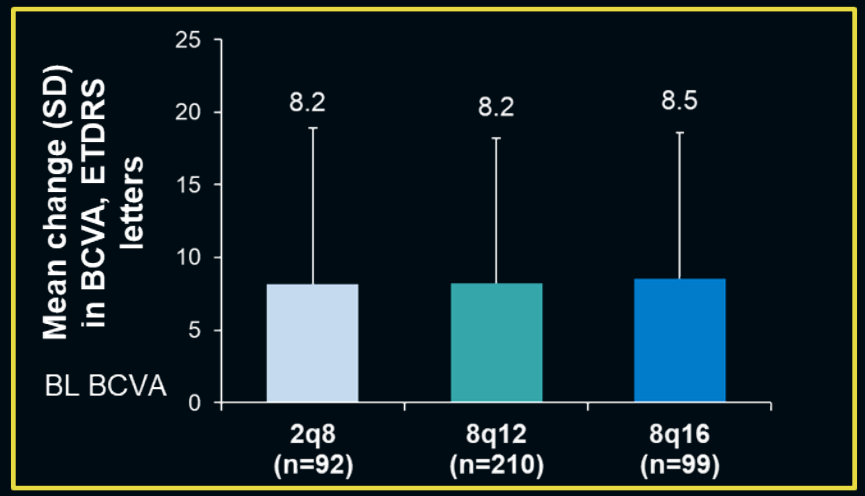


≥65-<75 years

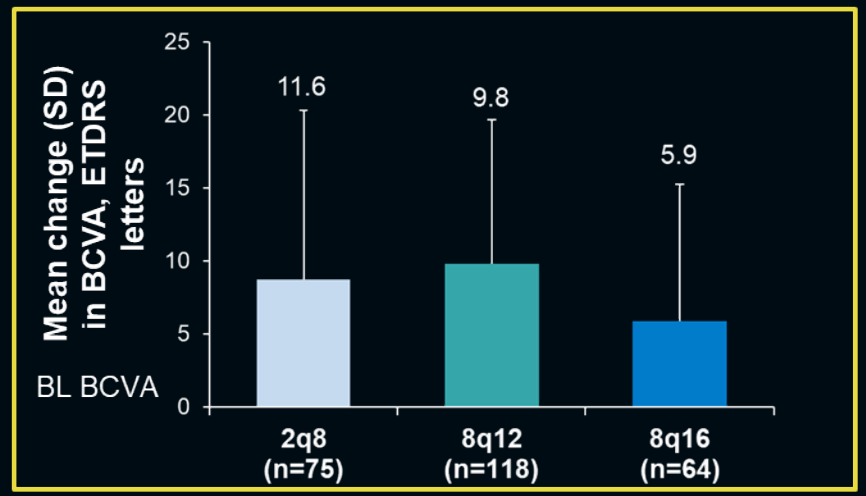


Sex

Male



Female



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

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

Mean Change in BCVA and Proportion of 8 mg Patients Who Maintained Randomized Dosing Interval Through Week 96 by Race[a]

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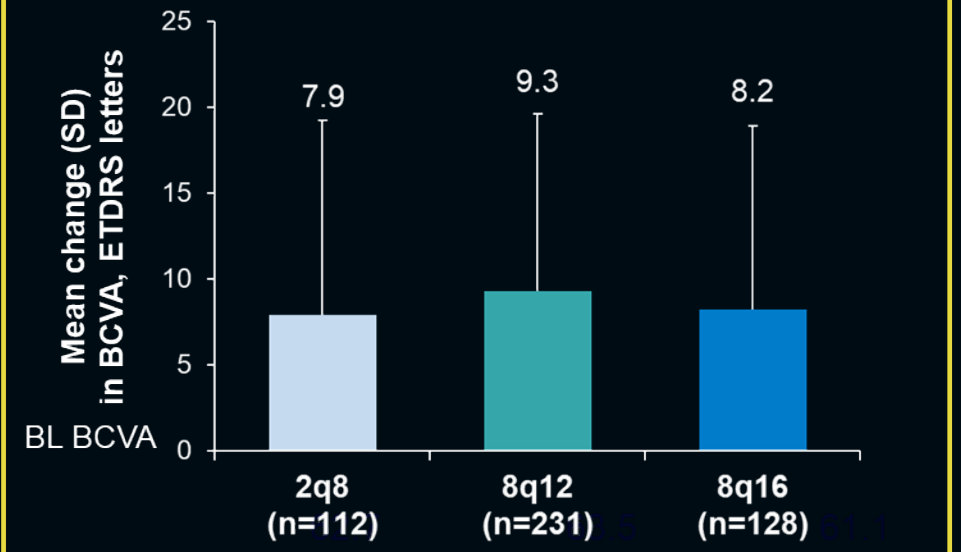
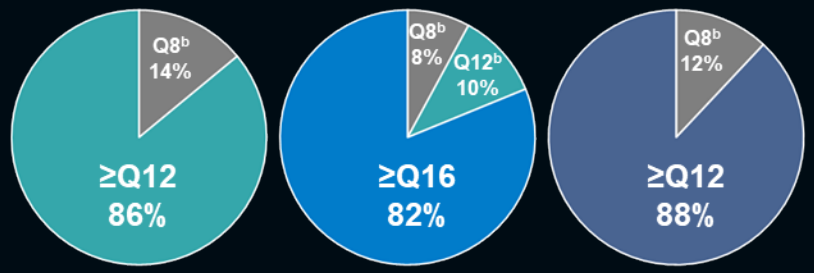
DME

White

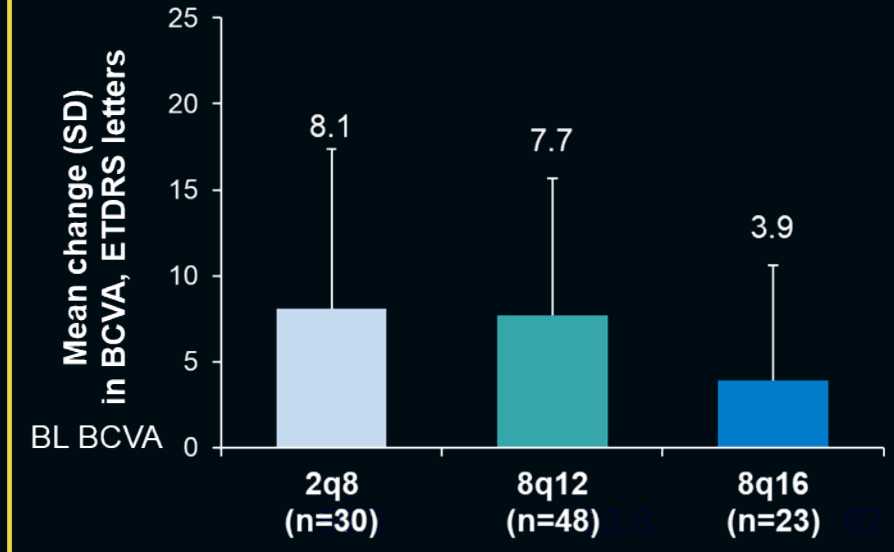


Proportion of 8 mg patients who maintained randomized dosing interval through Week 96

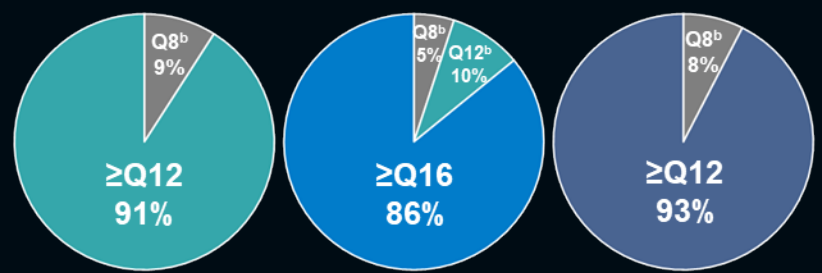


8q12 (n=177)[c] | 8q16 (n=108)[c] | All 8 mg (n=285)[c]

Asian



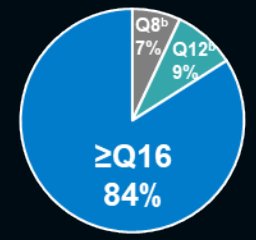
Proportion of 8 mg patients who maintained randomized dosing interval through Week 96



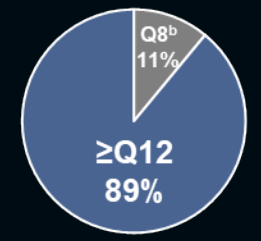
8q12 (n=46)[c] | 8q16 (n=21)[c] | All 8 mg (n=67)[c]

Proportion of all 8 mg patients who maintained randomized dosing interval through Week 96

8q12 (n=256)[c]



8q16 (n=139)[c]



All 8 mg (n=395)[c]

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

Mean Change in BCVA and Proportion of 8 mg Patients Who Maintained Randomized Dosing Interval Through Week 96 by Baseline BCVA

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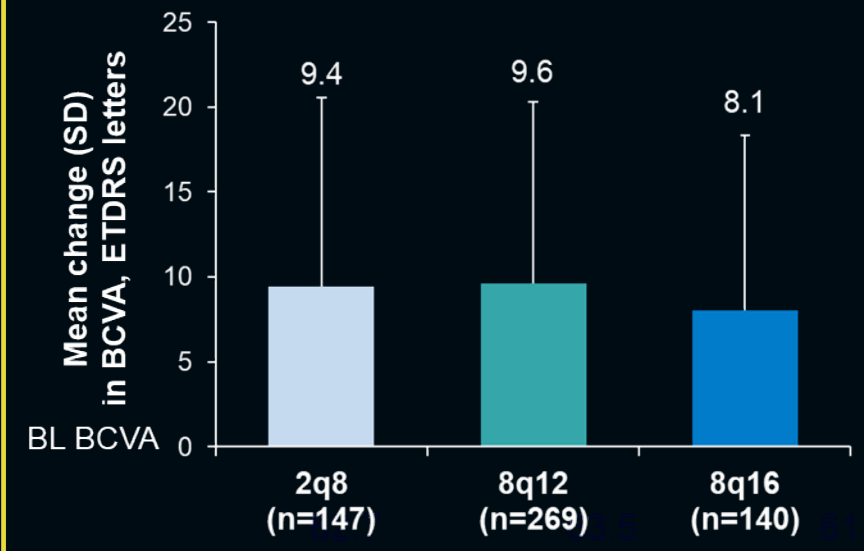
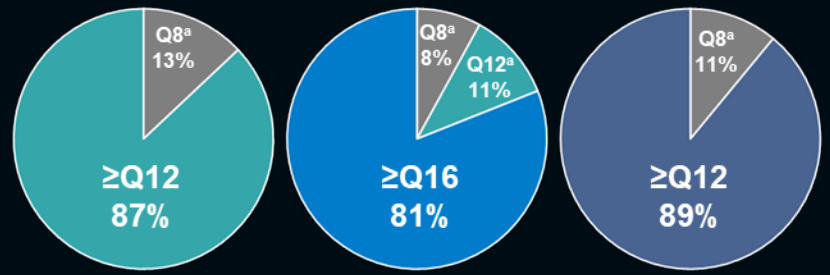
DME

Baseline BCVA ≤73 letters

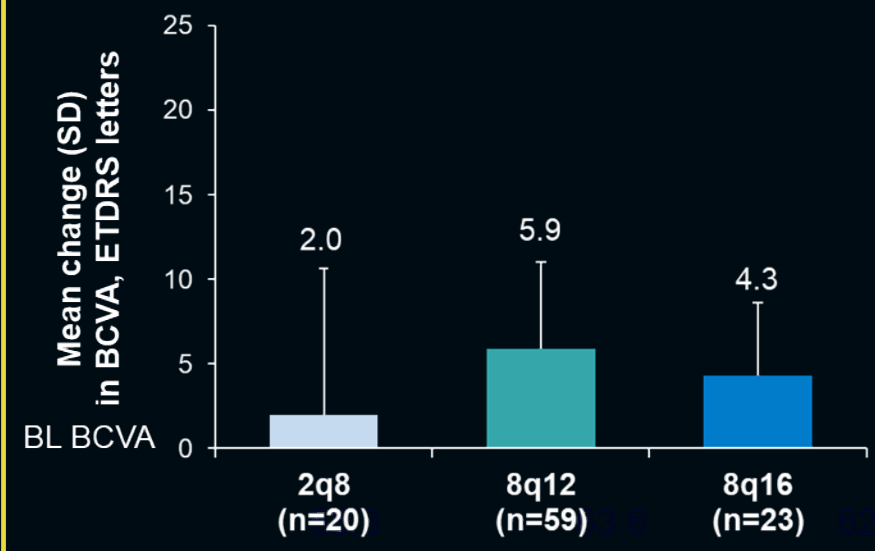


Proportion of 8 mg patients who maintained randomized dosing interval through Week 96

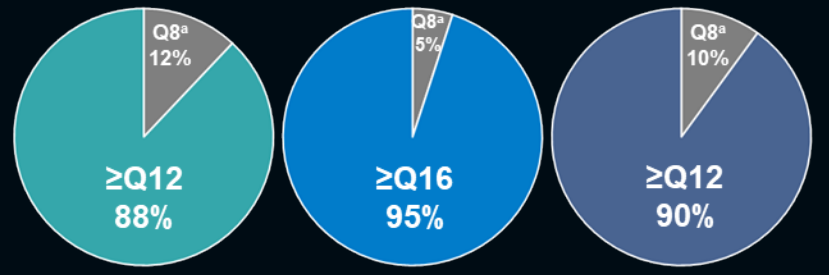


8q12 (n=207)[b] 8q16 (n=118)[b] All 8 mg (n=328)[b]

Baseline BCVA >73 letters



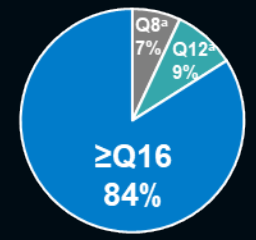
Proportion of 8 mg patients who maintained randomized dosing interval through Week 96



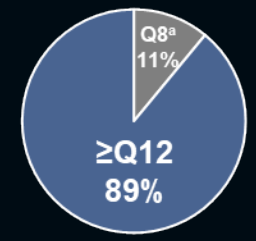
8q12 (n=49)[b] 8q16 (n=21)[b] All 8 mg (n=70)[b]

Proportion of all 8 mg patients who maintained randomized dosing interval through Week 96

8q12 (n=256)[b]



8q16 (n=139)[b]



All 8 mg (n=395)[b]

FAS, observed cases (censoring data post-ICE). At BL, 2q8: n=167; 8q12: n=328; 8q16: n=163.
[a]Patients shortened based on DRM criteria through Week 96; [b]Patients completing Week 96. Values may not add up to 100% due to rounding.

Mean Change in BCVA and Proportion of 8 mg Patients Who Maintained Randomized Dosing Interval Through Week 96 by Baseline CRT

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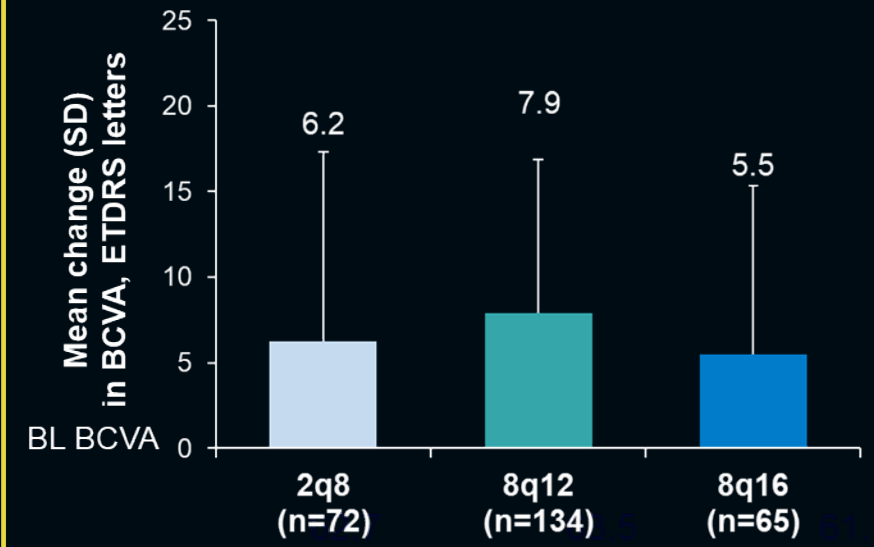
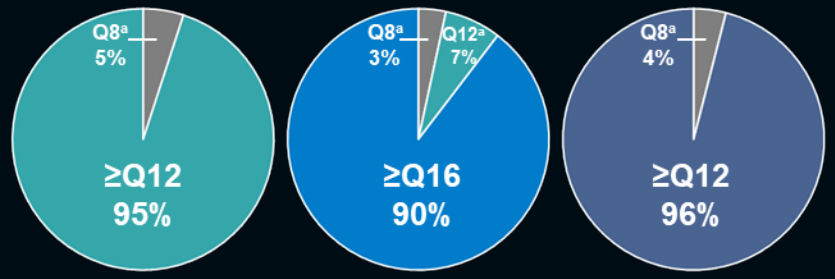
DME

Baseline CRT <400 µm

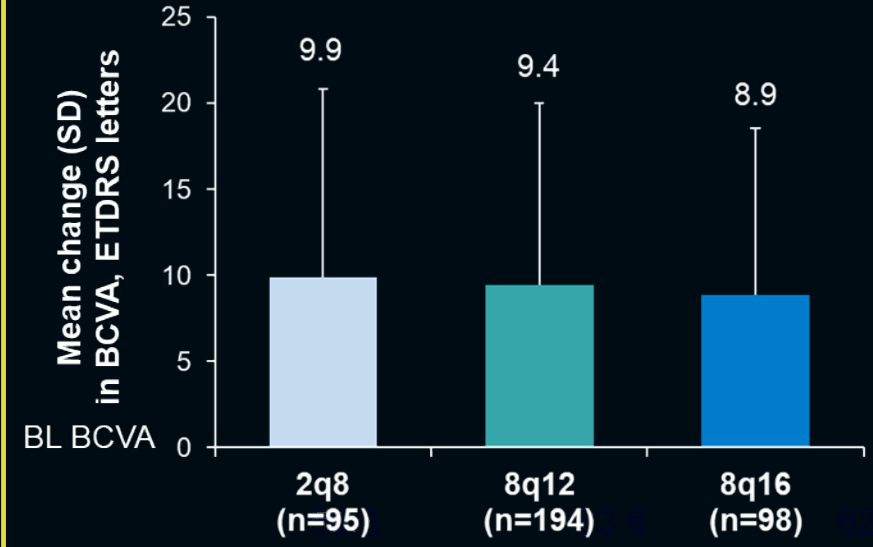


Proportion of 8 mg patients who maintained randomized dosing interval through Week 96

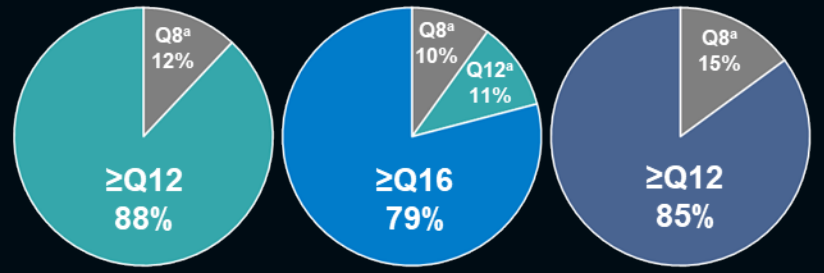


8q12 (n=102)[b] | 8q16 (n=58)[b] | All 8 mg (n=160)[b]

Baseline CRT ≥400 µm



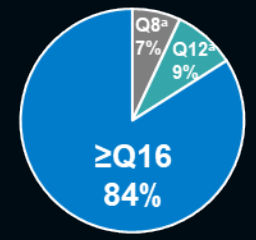
Proportion of 8 mg patients who maintained randomized dosing interval through Week 96



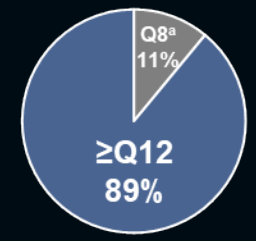
8q12 (n=154)[b] | 8q16 (n=81)[b] | All 8 mg (n=235)[b]

Proportion of all 8 mg patients who maintained randomized dosing interval through Week 96

8q12 (n=256)[b]



8q16 (n=139)[b]



All 8 mg (n=395)[b]

FAS, observed cases (censoring data post-ICE). At BL, 2q8: n=167; 8q12: n=328; 8q16: n=163.
[a]Patients shortened based on DRM criteria through Week 96. [b]Patients completing Week 96. Values may not add up to 100 due to rounding.

Conclusions

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DME

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