Intravitreal Aflibercept 8 mg for Diabetic Macular Edema: Week 48 Efficacy Outcomes by Baseline Demographics in the Phase 2/3 PHOTON Trial

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Disclosures

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DME

- Jean-Francois Korobelnik receives consultant fees for AbbVie, Apellis, Bayer, Janssen, Nano Retina, Roche, Théa Pharmaceuticals, and Carl Zeiss Meditec AG; and is a member of a data safety monitoring board or advisory board for Alexion, Novo Nordisk, and Oxular
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- The results of this analysis were previously presented at the ASRS Annual Meeting, July 28–Aug 1, 2023
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PHOTON: Study Design and Dosing Schedule

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DME

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

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

	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 (n=167)	X	X	X	X	X	o	X	o	X	o	X	o	X
8q12 (n=328)	X	X	X	o	o	X	o	o	X	o	o	X	o
8q16 (n=163)	X	X	X	o	o	o	X	o	o	o	X	o	o

Note: Aflibercept 2 mg arm received 5 initial monthly injections versus aflibercept 8 mg arms, which received only 3 initial monthly injections

DRM Criteria for Shortening Dosing Interval

- **>10-letter loss in BCVA compared to Week 12, due to persistent or worsening DME**

AND

- **>50 µm increase in CST compared to Week 12**

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 40 for 8q16: Treatment interval shortened by 4 weeks for patients meeting DRM criteria

Stippled boxes = initial treatment phase; X = active injection; o = sham injection. Note: Figure does not reflect all dosing options once a patient's dosing interval is shortened.
[a]Treatment naïve and pre-treated.
2q8, aflibercept 2 mg every 8 weeks; 8q12, aflibercept 8 mg every 12 weeks; 8q16, aflibercept 8 mg every 16 weeks; BCVA, best-corrected visual acuity; CST, central subfield thickness; DME, diabetic macular edema; DRM, dose regimen modification; DRSS, Diabetic Retinopathy Severity Scale; Q8, every 8 weeks; Q12, every 12 weeks; Wk, week.

Baseline Demographics

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DME

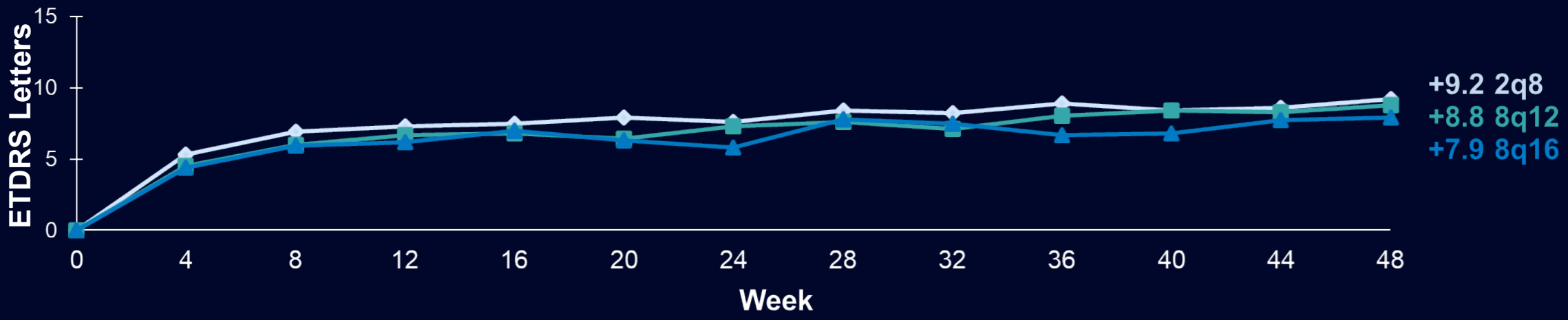
	2q8	8q12	8q16	Total
N (FAS/SAF)	167	328	163	658
Age, years	63.0 (9.8)	62.1 (11.1)	61.9 (9.5)	62.3 (10.4)
Female, %	44.9%	36.0%	39.3%	39.1%
Race, %				
White	67.1%	70.4%	78.5%	71.6%
Black or African American	10.8%	10.7%	5.5%	9.4%
Asian	18.0%	14.6%	14.1%	15.3%
Other	2.4%	3.0%	0.6%	2.4%
Not reported	1.8%	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)
BMI, kg/m^2	29.9 (6.5)	30.4 (6.2)	31.0 (6.1)	30.5 (6.2)
Prior treatment for DME, %	44.3%	43.6%	43.6%	43.8%
BCVA, ETDRS letters	61.5 (11.2)	63.6 (10.1)	61.4 (11.8)	62.5 (10.9)
CST, µm	457.2 (144.0)	449.1 (127.4)	460.3 (117.8)	454.0 (129.5)

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

Mean Change in BCVA Through Week 48

DME

BCVA Change from Baseline[a]

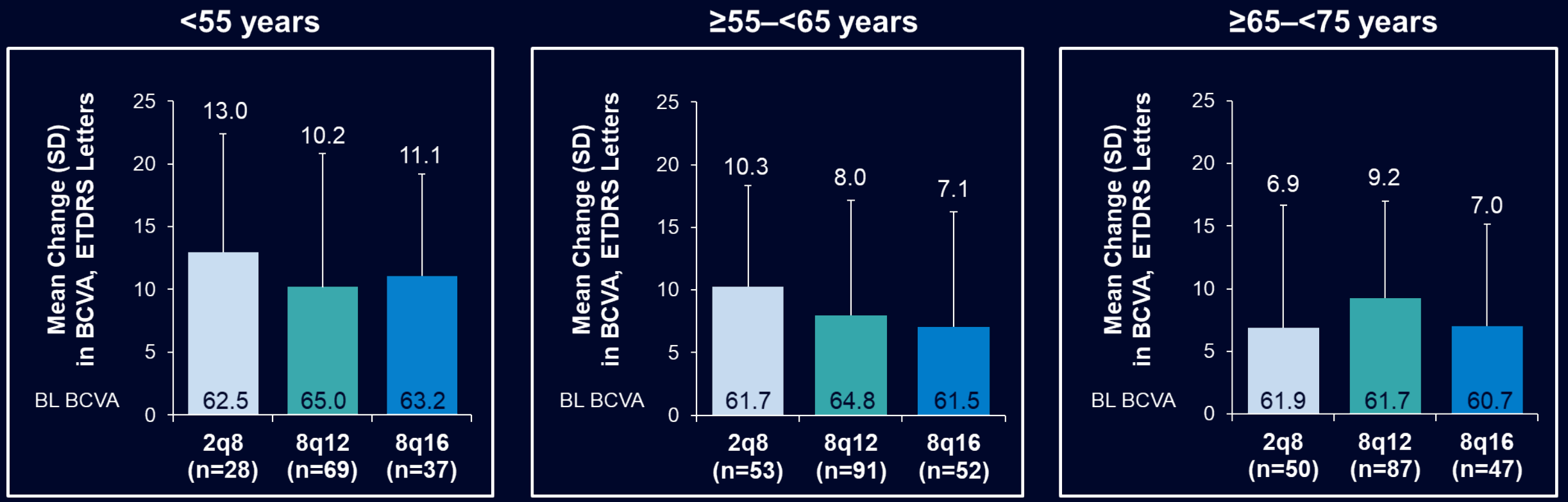


	LS mean change from BL[b]	Difference in LS means vs aflibercept 2q8	Two-sided 95% CI	One-sided test for non-inferiority at four-letter margin
2q8	8.7	—	—	—
8q12	8.1	−0.57	−2.26, 1.13	p < 0.0001
8q16	7.2	−1.44	−3.27, 0.39	p = 0.0031

[a]Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at BL).
[b]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 BL BCVA as a covariate, treatment group (aflibercept 2q8, 8q12, 8q16) and stratification variables (geographic region [Japan vs rest of the world], BL CST [<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. BL, baseline; ICE, intercurrent event; LS, least squares; MMRM, mixed model for repeated measures.

Mean Change in BCVA at Week 48 by Age[a]

DME

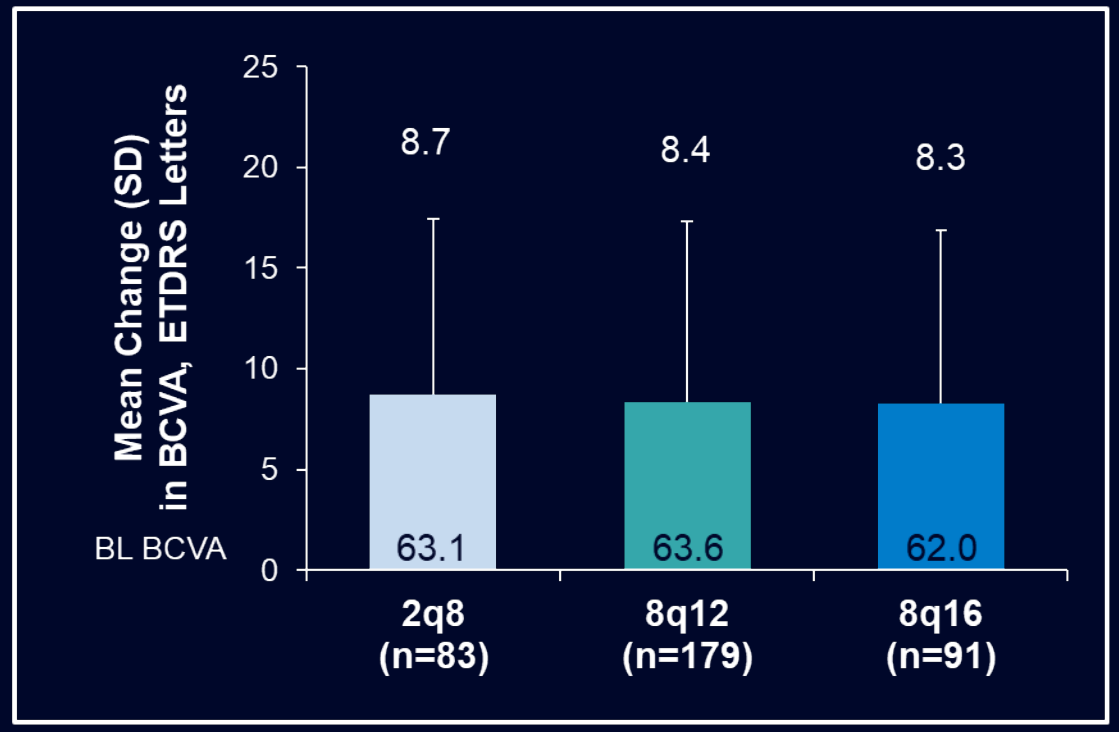


FAS.
[a]The subgroup age ≥75 years could not be evaluated due to small sample size (<15 patients in the 8q16 treatment group).
Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at BL).

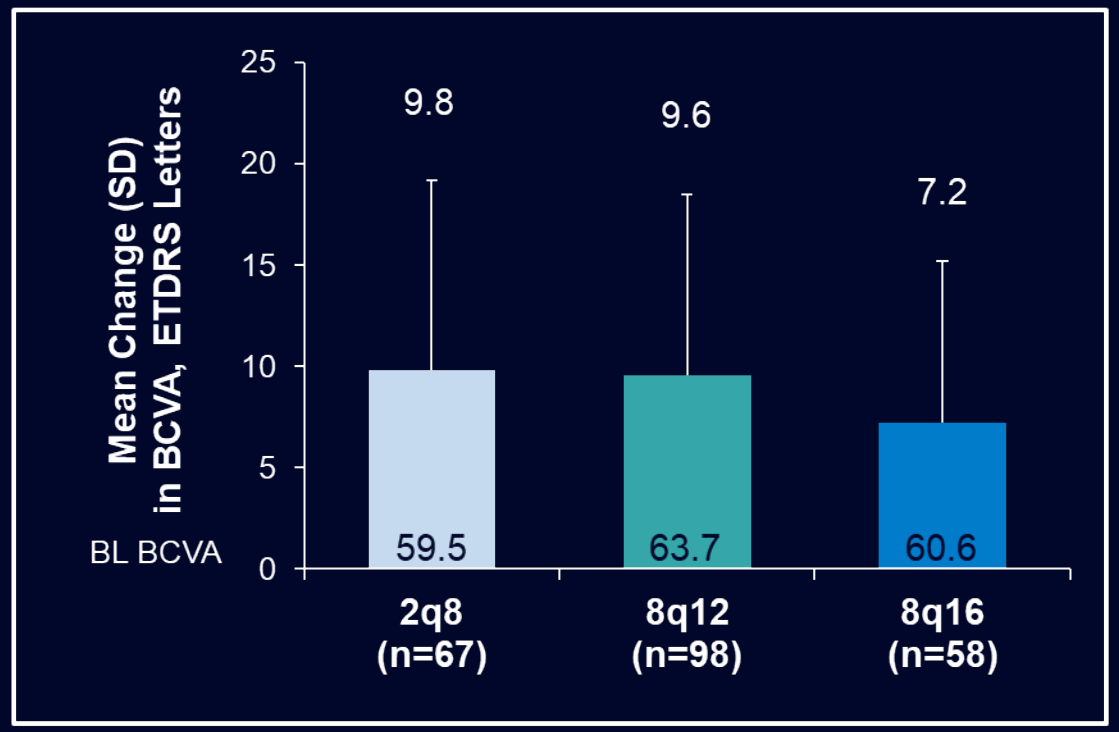
Mean Change in BCVA at Week 48 by Sex

DME

Male



Female

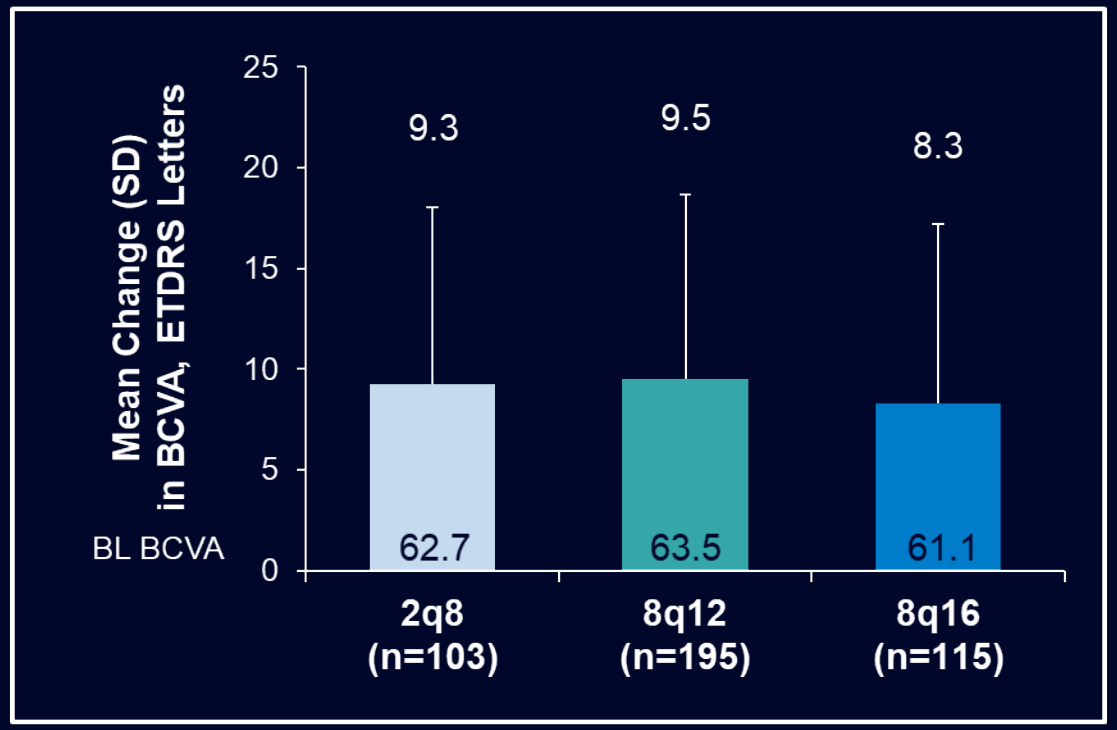


FAS.
Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at BL).

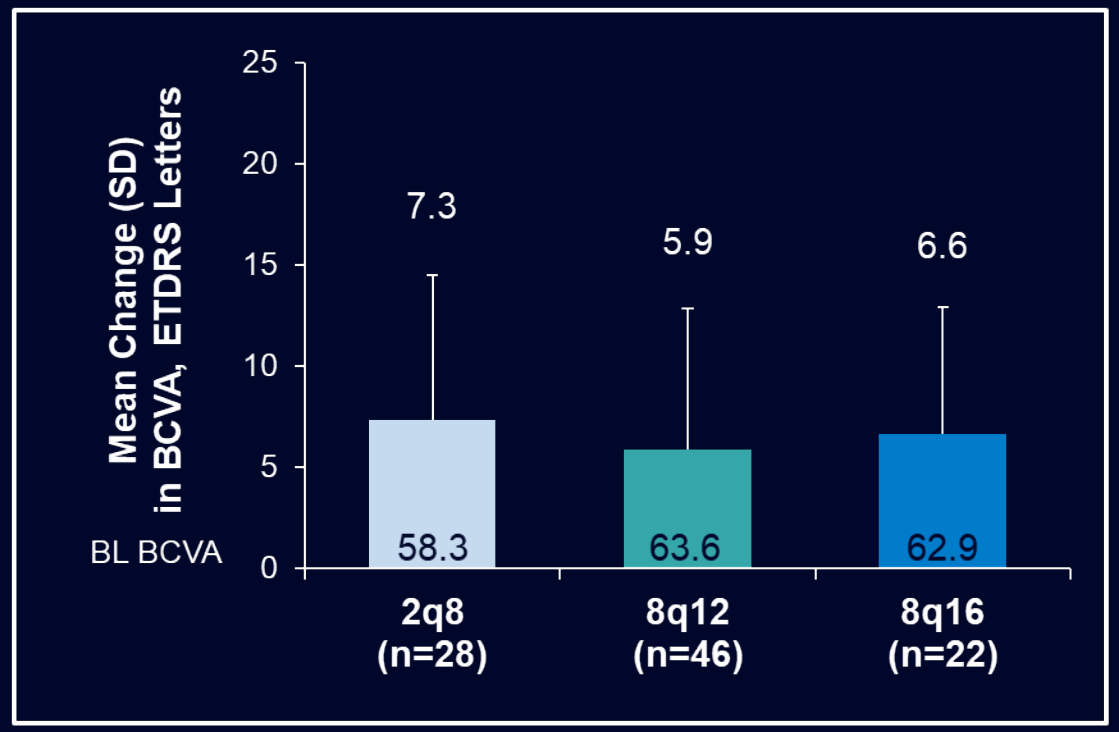
Mean Change in BCVA at Week 48 by Race[a]

DME

White



Asian

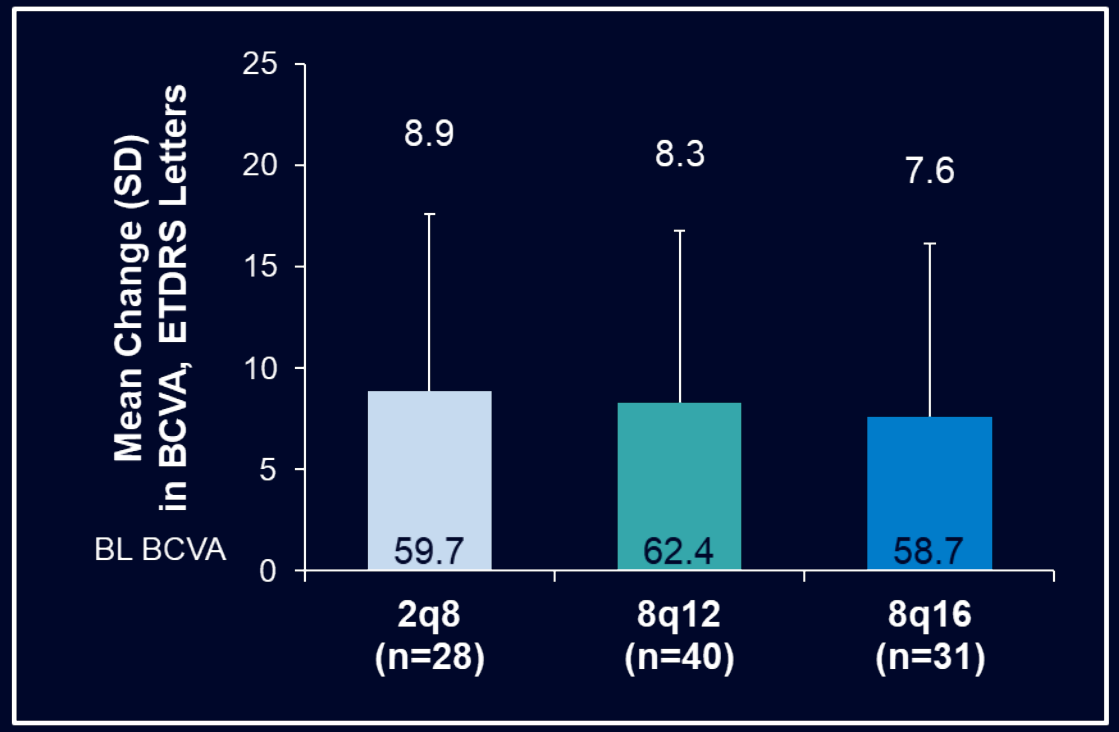


FAS.
[a]The subgroup Black or African American race could not be evaluated due to small sample size (<15 patients in the 2q8 and 8q16 groups).
Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at BL).

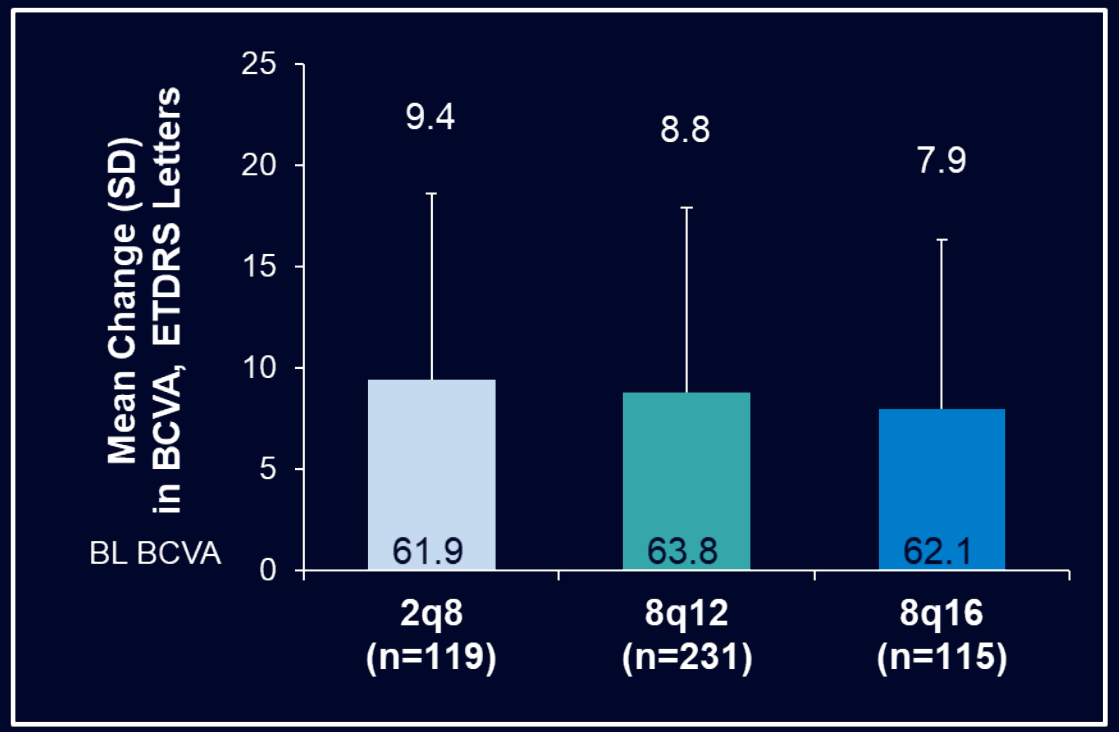
Mean Change in BCVA at Week 48 by Ethnicity

DME

Hispanic or Latino



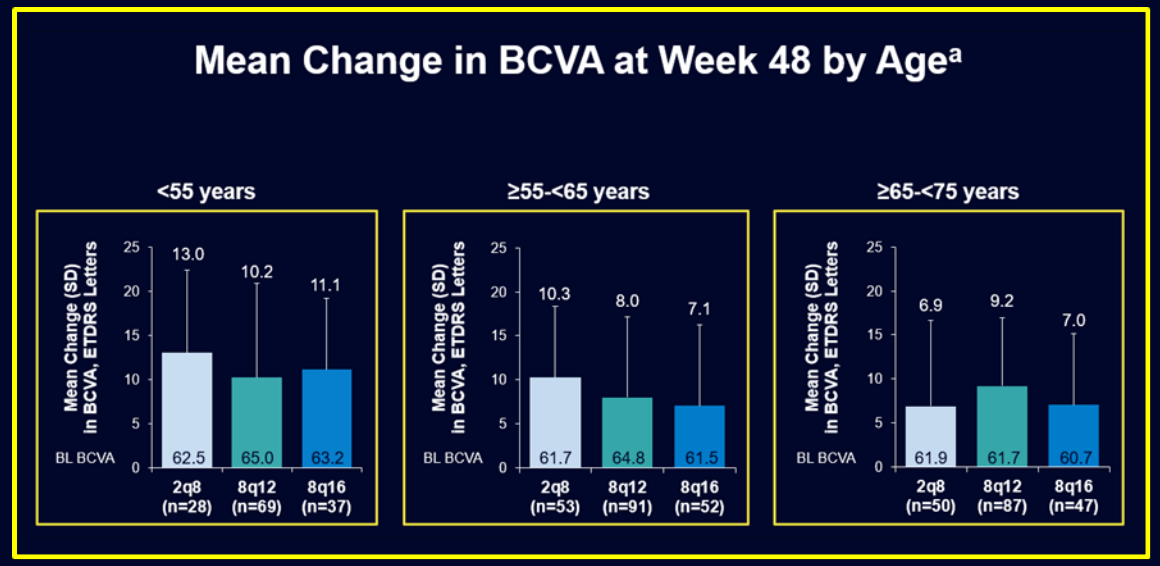
Not Hispanic or Latino

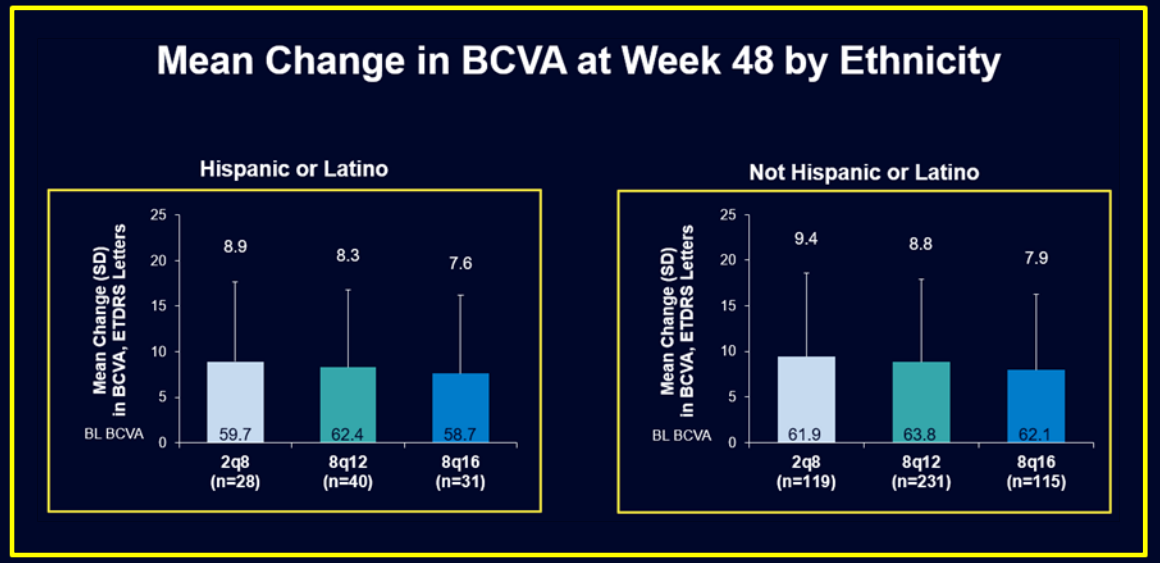


FAS.
Observed values (censoring data post-ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at BL).

Conclusions

DME





- Aflibercept 8 mg achieved meaningful BCVA gains from baseline at Week 48 in patients with DME across evaluable subgroups of age, sex, race, and ethnicity
- Limitations: this analysis was not designed to evaluate statistical differences within subgroups, and select subgroups (age ≥75 years and Black or African American race) could not be evaluated due to small sample size